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Advanced / Intensive Courses 2020/21

Winter term 2020/2021:
1st Half
09.11.20 – 18.12.20  Collective Animal Behavior (Couzin, Jordan)
09.11.20 – 18.12.20  Human and Environmental Toxicology (Dietrich)
09.11.20 – 18.12.20  Environmental Genomics (Epp)
09.11.20 – 18.12.20  Immunology (Groettrup, Schmidtke)
11.11.20 – 22.12.20  Molecular Genetics: Cell cycle regulation – from mechanisms to disease (T. Mayer)

2nd Half  (*advanced course will exceed the semester end for one week)
04.01.21 – 12.02.21  Molecular Toxicology & Bioimaging (Bürkle, May, Mangerich)
04.01.21 – 12.02.21  Cell Biology – Cell Adhesion and Signal Transduction (Hauck)
04.01.21 – 12.02.21  Bioinformatics and X-Ray Structural Analysis (Mayans, Diederichs)
04.01.21 – 12.02.21  Microbial Ecology and Limnic Microbiology (Schleheck)
04.01.21 – 12.02.21  Chemical Ecology (Spiteller)
04.01.21 – 12.02.21  The role of microbes in stress response and resilience of aquatic metaorganisms (Voolstra)
04.01.21 – 12.02.21  Organismal biology: Going wild (Wikelski, Dechmann. Aplin)
delayed 22.02.21 – 02.04.21
11.01.21 – 19.02.21  Novel in vitro Methods in Pharmacology & Toxicology (Leist)

Summer term 2021:
1st Half
06.04.21 – 28.05.21  Quantitative tools for behavioral ecologists
includes field research in behavioral ecology
(Crofoot, Strandburg Peshkin, Jordan, Kalbitzer)
19.04.21 – 28.05.21  Theoretical and Experimental Ecology and Evolution (Becks)
19.04.21 – 28.05.21  Biochemical Pharmacology (Brunner)
19.04.21 – 28.05.21  Physiology and Biochemistry of Plants (Isono, Nagel)
19.04.21 – 28.05.21  Physiology, Ecology and Molecular Biology of Algae (Kroth)
19.04.21 – 28.05.21  Molecular Evolutionary Biology (Meyer)
(31.05.21 - 06.06.21 Pentecost)

2nd Half
14.06.21 – 23.07.21  Molecular Microbiology and Cell Biology: Chaperone functions in health and disease (Deuerling)
14.06.21 – 23.07.21  Behavioral Neurobiology (Kleineidam, Bahl and others)
14.06.21 – 23.07.21  Global change ecology and plants (van Kleunen and others)
14.06.21 – 23.07.21  Dynamics of aquatic ecosystems (Peeters)
14.06.21 – 23.07.21  Cellular Biochemistry (Scheffner)
14.06.21 – 23.07.21  Biochemistry and Mass Spectrometry (Stengel)
Advanced / Intensive Courses 2021/22

Winter term 2021/2022:

1st Half
08.11.21 – 17.12.21 Collective Animal Behavior (Couzin, Jordan)
08.11.21 – 17.12.21 Human and Environmental Toxicology (Dietrich)
08.11.21 – 17.12.21 Environmental Genomics (Epp)
08.11.21 – 17.12.21 Immunology (Groettrup, Schmidtke)
08.11.21 – 17.12.21 Applied Bioinformatics for Studying Health and Disease (Gruber)
08.11.21 – 17.12.21 Advanced Technologies for the Life Sciences (Core Facility Leaders)
08.11.21 – 17.12.21 Molecular Genetics: Cell cycle regulation – from mechanisms to disease (T. Mayer)

2nd Half (*advanced course will exceed the semester end for one week)
03.01.22 – 11.02.22 Molecular Toxicology (Bürkle, Mangerich)
10.01.22 – 18.02.22* Cell Biology – Cell Adhesion and Signal Transduction (Hauck)
10.01.22 – 18.02.22* Novel in vitro Methods in Pharmacology & Toxicology (Leist)
10.01.22 – 18.02.22* Bioinformatics and X-Ray Structural Analysis (Mayans, Diederichs)
10.01.22 – 18.02.22* Microbial Ecology and Limnic Microbiology (Schleheck)
10.01.22 – 18.02.22* Chemical Ecology (Spiteller)
10.01.22 – 18.02.22* The role of microbes in stress response and resilience of aquatic metaorganisms (Voolstra)
10.01.22 – 18.02.22* Organismal biology: Going wild (Wikelski, Dechmann. Aplin)

Summer term 2022:

1st Half
04.04.22 – 27.05.22 Quantitative tools for behavioral ecologists includes field research in behavioral ecology (Crofoot, Strandburg Peshkin, Jordan, Kalbitzer)
18.04.22 – 27.05.22 Theoretical and Experimental Ecology and Evolution (Becks)
18.04.22 – 27.05.22 Biochemical Pharmacology (Brunner)
18.04.22 – 27.05.22 Physiology and Biochemistry of Plants (Isono, Nagel)
18.04.22 – 27.05.22 Physiology, Ecology and Molecular Biology of Algae (Kroth)
18.04.22 – 27.05.22 Molecular Evolutionary Biology (Meyer)

2nd Half (* with 1 week break 13.06.22 - 17.06.22 = Pentecost)
07.06.22 – 22.07.22* Molecular Microbiology and Cell Biology: Chaperone functions in health and disease (Deuerling)
07.06.22 – 22.07.22* Dynamics of aquatic ecosystems (Peeters)
07.06.22 – 22.07.22* Cellular Biochemistry (Scheffner)
07.06.22 – 22.07.22* Biochemistry and Mass Spectrometry (Stengel)
20.06.22 – 29.07.22 Behavioral Neurobiology (Kleineidam, Bahl and others)
20.06.22 – 29.07.22 Global change ecology and plants (van Kleunen and others)
Advanced course "Theoretical and Experimental Ecology and Evolution"

Coordinator: Prof. Dr. Lutz Becks

1. Introduction

We are interested in the basic processes and mechanisms of species interactions that drive ecological and evolutionary changes over time and space. Species interactions such as between predator and prey, host and pathogen, competitors and symbionts are an integral part of any community and are the major drivers of evolutionary and ecological changes. They often exert strong selection on the interacting species, leading to rapid and significant evolutionary changes in important traits like anti-predatory defenses, resistance or a shift in resource usage. At the same time, species interactions typically result in significant and rapid changes in population sizes, with for example regular or irregular fluctuations in population sizes or the extinction of a population. Different processes and mechanism can drive and regulate the evolutionary and ecological changes (e.g., density-dependent and frequency-dependent processes) and several occur typically simultaneously and influence each other.

Over the last years, it became more and more apparent that rapid evolutionary change (i.e., within a few generations) is an important driver for ecological changes and vice versa, which has led to the development of the research field of eco-evolutionary dynamics. In this important and rapidly growing research field, we aim to understand the importance of these eco-evolutionary dynamics. Understanding the mechanisms and processes that control ecological and evolutionary changes is important to predict how populations or communities react to environmental changes.

In our research we combine experimental approaches (e.g., experimental evolution where we can observe evolutionary change in real time) with mathematical modelling and sequencing approaches to test hypotheses and mechanisms that determine changes in population sizes and traits over time and space. We work with plankton communities and study predator-prey, host-virus, mutualistic and competitive interactions, as well as the combination of those.

2. Objectives

You will learn

- about the novel research field of eco-evolutionary dynamics
- ecological and evolutionary theory, community ecology
- to identify research question and design your own experiments and analyses of mathematical model to answer research questions
- a large range of methods used in ecology and evolution
3. Contents of the course

The course includes lectures, practicals, seminars and a fieldtrip. The lectures will introduce you to the important theories of ecology and evolution with respect to species interactions in communities as well as eco-evolutionary dynamics. In the practicals, you will learn experimental design, mathematical modelling, statistical analyses, scientific writing and presentation. We will teach you how to work with planktonic and microbial communities (culture methods; experimental evolution; enumeration by quantitative PCR methods, flow cytometry, automated High Content Microscopy, optical density measurements) as well as running analyses of mathematical models in R. During the seminars you will read and discuss recent scientific publications. Based on seminars and lectures, you will identify a research question, design and run your own experiment and model analyses in groups of two to put the skills and knowledge into practice.

4. Requirements

Interest and basic knowledge in ecology and evolution.

5. Exam

To pass the course, you have to be actively participating, present and discuss during seminars as well as your project results (poster), and write a paper on your research project.

For more information on our group, visit our webpage (https://www.limnologie.uni-konstanz.de) or contact lutz.becks@uni-konstanz.de
Advanced Course "Biochemical Pharmacology"

Coordinators:   Prof. Dr. Thomas Brunner  
                Dr. Paola Ripani  
                Dr. Anna Pia Plazzo

1. Introduction

The course intends to introduce various theoretical and research-associated aspects in 
the field of biomedicine, especially biochemistry, pharmacology, cell biology and 
inflammation. The compact course contains lectures, seminars, journal presentations 
and practical work in the laboratory under the guidance of members of the research 
group.

2. Content of the compact course

a) Theoretical part:

The theoretical part consists of lectures and seminars. In the first week the scientific 
background of the research conducted at the chair of biochemical pharmacology will be 
introduced in a possibly interactive manner. The lectures aim at introducing the scientific 
background, the different seminars specific research topics and projects, while in the 
journal clubs recent literature in the field will be presented and discussed. The lectures 
continue in the following weeks with 1.5 hours lectures daily in the morning.

The following subjects will be discussed:

- General lab safety
- Apoptosis-Necrosis-programed necrosis
- Detection methods of cell death
- The extrinsic apoptosis pathway-TNF Receptor family
- The intrinsic apoptosis pathway-Bcl-2 family
- Flow cytometry
- Immunopathologies of the intestine, skin and liver
- Immune homeostasis in the intestine
- Inflammatory bowel disease
- Steroid synthesis
- Extra-adrenal steroid synthesis in the intestine, lung and skin
- Nuclear receptors
- Tumor biology
- Pharmacology

The journal clubs consists of the presentation and discussion of recent publications of 
subjects covered by this advanced course. The publications will be presented by the 
participating students, with the aim to analyze and interprete scientific publications. 
Finally, each student will discuss the data obtained during the practical work of the 
course in a short presentation at the end of the course.
b) Practical part

In the practical part, the participating students will work on small projects, which are integrated into general projects and research topics of our research group. Students will be coached and supervised by postdocs, PhD students and master students, working on these specific subject, aiming at introducing the students to various aspects of biochemical, cell biological and pharmacological research in an intense and realistic manner. The goal is to give the participating students a deeper insight into the planning, conduction, analysis and interpretation of experiments and research projects. With the participation in this Advanced Course the students should obtain basic skills for future scientific work during the Master thesis.

Actual research subjects at the chair of biochemical pharmacology:

- Regulation of apoptotic and necrotic cell death in tumor cells and primary cells
- Interaktion between the extrinsic and intrinsic apoptosis pathway
- Activation of Bcl-2 homologs
- Thiazolides, Glutathion-S-transferase P1 and apoptosis in colon carcinoma cells
- Regulation of extra-adrenal glucocorticoid synthesis in intestine, lung and skin
- Role of extra-adrenal glucocorticoid synthesis in the regulation of immune homeostasis
- Regulation of steroid synthesis by nuclear receptors
- The role of nuclear receptors in the regulation of apoptotic cell death
- Primary intestinal and tumor organoids

Used techniques:

- Biochemical and molecular standard methods
- Isolation, culture, activation and analysis of primary cells
- Organ cultures of lung and intestinal tissue
- Culture and transfection of cell lines
- Apoptosis assays
- Flow cytometry for the phenotyping and sorting of immune cells
- Detection of proteins and their activation by Western blotting
- Luciferase reporter assays to study gene regulation
- Radioimmunoassay
- Immunofluorescence and immunohistochemistry
- Microscopy and histology
- Laser Capture Microdissection
- Quantitative PCR

3. Expected background knowledge

Basic knowledge in biochemistry, immunology and molecular biology is expected.
4. Literature

**General literature:**


**Specific literature:**

Advanced Course „Molecular Toxicology & Bioimaging”

Coordinators: Prof. Alexander Bürkle, Prof. Elisa May, PD Dr. Aswin Mangerich

1. Introduction

This Advanced Course provides a basis for future research and application-oriented work in the field of biomedicine, in particular molecular toxicology. The students will gain insights into the theory and practice of molecular toxicology and into novel imaging approaches within this field.

2. Content

   a. Theoretical part

   - The focus of our highly interactive lectures is the recapitulation and deepening of knowledge in the field of molecular toxicology with emphases on DNA damage and repair, aging and cancer biology, and biomaging techniques. In an interactive Journal Club session the students are trained to extract knowledge from a current original publication about research in the field. Another important component is the preparation of posters on current methods in molecular toxicology and bioimaging and their presentation during three poster sessions, with (real) prizes awarded for the best posters.

   Topics of the lectures include the following:
   - DNA damage and DNA repair pathways
   - NAD metabolism and poly(ADP-ribosyl)ation
   - DNA replication and replication stress
   - Imaging of DNA damage and repair
   - Molecular mechanisms and biomarkers of ageing
   - Molecular toxicology of sulfur mustard and other DNA crosslinking agents
   - Introduction into cytostatic agents and cancer therapies
   - Laboratory safety, including fire protection, chemical safety and biohazards

   b. Practical part

   In the practical part of the course the students are directly integrated into the current research projects in our groups. Each student will work on his/her own mini project under the guidance of an assigned tutor (postdoc or PhD student), the supervision being mostly on 2:1 basis. Thus, very intensive training is guaranteed and students will get a realistic, hands-on experience of all facets of scientific activity in the field, in particular regarding the design, planning and running of experiments, data evaluation and interpretation, self-criticism, trouble shooting, and written and oral reporting of results. As a result, the students will acquire the ability to conduct independent research work in the field of molecular toxicology and bioimaging.

   Our current research projects include the following:
   - Biochemistry and cell biology of NAD⁺ metabolism and poly(ADP-ribosyl)ation
• Cell and molecular biology of DNA replication stress and the relevance of chromatin architecture
• Development of photomanipulation assays for DNA repair research (cooperation with the Dept of Physics)
• Biochemical and functional assays for monitoring DNA damage and DNA repair in living cells
• Molecular mechanisms of toxicity induced by DNA crosslinking agents
• Relevance of DNA damage and DNA repair for the ageing process
• Establishment of biomarkers of ageing

Apart from standard methods of biochemistry and molecular biology, the following specific methodology will be applied:
• Quantification of DNA strand breaks and other DNA lesions by using an automated device (“FADU robot”) developed by us
• Preparation and fractionation of poly(ADP-ribose)
• Characterisation of poly(ADP-ribose) by ESI mass spectrometry
• Flow cytometry
• Bacterial overexpression and purification of recombinant proteins
• DNA damage induction in living cells using ultrashort laser pulses
• Fluorescence imaging of DNA repair processes in real time

3. Requirements

Successful participation in modules like „Einführung in die Medizin / Humanbiologie“ and „Pharmakologie und Toxikologie I“ during Bachelor Studies.

Recommended Literature
**Advanced Course „Advanced Technologies for the Life Sciences“**

**Dieser Kurs entfällt!**

Offered by the Core Facilities (Gerätezentren) of the Department of Biology:
Bioimaging Center (BIC)
Electron Microscopy Center (EMC)
Flow Cytometry Facility (FlowKon)
Next-Generation Sequencing Facility (SequAna)

Number of Students: 12

This pilot Advanced Course offers the student insights into four technologies broadly used in life science research: electron and light microscopy, flow cytometry, and next-generation sequencing. After the first week of lectures and active learning assignments, students will start a four-week rotation during which they will stay in each facility for one week in groups of three. During the final week, they will give presentations, prepare their reports, and give feedback for the evaluation. The course aims to give students basic theoretical background and first hands-on experiences in all four technologies, make them aware of their limitations and potential, and introduce them to the working environment of research infrastructures.

**BIC: Light Microscopy**
The BIC will give students an overview of the current light microscopy approaches, e.g. polarization microscopy, fluorescence microscopy (widefield illumination and laser scanning), holographic microscopy. Lectures will introduce the different methods, explain the fundamental principles and their applications and limitations. They will also introduce approaches to assess the microscope performance and cover ethical and data management issues when working with scientific image data. In hands-on assignments, students will learn how to prepare biological samples for different imaging approaches, carry out microscopy performance checks, or perform image analysis tasks.

**EMC: Electron Microscopy**
The EMC will introduce techniques and methods used in electron microscopy through lectures, demonstrations, and hands-on exercises in short students projects. Using different biological samples the following techniques in electron microscopy will be covered: Scanning electron microscopy (SEM), transmission electron microscopy (TEM), energy-dispersive x-ray spectroscopy (EDX) and Focused Ion Beam (FIB). The short students’ hands-on projects will cover one or two of the above-named techniques, including methods for sample preparation from the living organism to the imaging and data analyses.

**Flowkon: Flow Cytometry**
The practical-oriented training course at the FlowKon will introduce techniques and methods used in flow cytometry. The theoretical part of the course outlines essential
principles of flow cytometers including optics, fluidics, and electronics, the properties of fluorophores and explains basic rules of panel design and compensation. The hands-on projects will cover common applications of flow cytometry and demonstrate instrument construction, operation, and data acquisition on different flow cytometric instruments.

SequAna: Sequence Analysis
The advent of next-generation sequencing (NGS) technologies over recent years have transformed the life sciences: an entire human genome can now be sequenced in a matter of days for US$1,000, changing the way we conduct research and analyze data. The new Sequencing Analysis (SequAna) Core Facility will introduce techniques and methods associated with NGS technologies, covering the wet lab (sequencing library generation and quality control) and in silico aspects (sequencing platforms, sequencing files, filtering/trimming/assembly/annotation of sequencing data). About 30% of the course will cover molecular biology wet lab techniques and the remaining 70% will cover bioinformatics analysis, mainly in the form of UNIX command line work. Students will become acquainted with common NGS workflows and data frameworks.
Advanced Course "Collective Animal Behavior"

Coordinator: Prof. Iain Couzin

Supervisors: Prof. Dr. Iain Couzin, Dr. Alex Jordan
(Chair of Biodiversity and Collective Behavior, University of Konstanz and Max Planck Institute of Animal Behavior)

Overview:

"This course will focus on the quantitative analysis of collective animal behavior in the laboratory and the field. Introductory lectures will cover key concepts and techniques, including automated tracking of animal movements and postures in 2D and 3D space, how social interactions scale to collective dynamics, how information flows through social networks and the resulting transmission of socially learned knowledge and the relation to cumulative culture in animal populations and societies. Theoretical concepts will be expounded through the development of simulations of collective dynamics using video game engines and immersive virtual reality. Subsequently students, and the faculty, will work together to design analyses of models or existing data, resulting in novel research projects.

Please check our website www.collectivebehavior.com for latest information about our current research."
Quantitative tools for behavioral ecologists

Instructors: Meg Crofoot, Alex Jordan, Urs Kalbitzer, Ariana Strandburg-Peshkin

This course will equip students with the analytical and experimental design skills needed to conduct research on the behavior and ecology of animals in the modern era. As part of a two-course sequence with the Field Research in Behavioral Ecology (led by Alex Jordan), this course will prepare students to conduct their own studies of animals in the wild. These two courses are co-requisite and must be taken together.

The course will be based around a series of hands-on modules in which students learn quantitative and programming skills by interacting with real biological data as well the basic concepts of behavioral ecology. Students will learn how to design studies to ask specific biological questions and how to wrangle, visualize, and interpret the resulting data to answer those questions. In conjunction with short lectures on important concepts in programming, data analysis, and the principles of behavioral ecology, they get to “play” with a variety of existing datasets from recent and current studies in behavioral ecology. They will then apply their skills by designing their own research projects to be carried out in the field.

This course will be taught primarily in R, but other programming languages, such as Python, will also be briefly introduced. It will build up from the basics, and no prior knowledge of programming is expected. Students should, however, bring enthusiasm for picking up new skills and a positive attitude towards diving into computational challenges.
Advanced Course "Molecular Microbiology and Cell Biology: Chaperone functions in health and disease"

Coordinator: Prof. Dr. E. Deuerling

Function and Mechanisms of Molecular Chaperones in Health and Disease

1. Introduction

The generation of biologically active proteins is a basic process which has to proceed in all cells – from bacteria to humans – with a maximum of precision to ensure the survival of the cell. The biosynthesis of proteins at the ribosomes is an exceedingly complex and fast process. For example, already in a bacterial cell approx. 30,000 new proteins per minute are produced at 20,000 ribosomes.

Proteins are functional – i.e. as enzymes or structural components – only if they adopt a defined three-dimensional structure (folding). Proteins are synthesized at the ribosomes as linear polymers composed of amino acids and fold into their defined three-dimensional structure after or during their synthesis. This folding crucially depends on supporting helper proteins, called the Molecular Chaperones. All cells contain a network of different chaperones which cooperate with each other and thus control and assist the folding processes in space and time. Hence, protein folding and the function of Molecular Chaperones are of fundamental importance for all fields of biology and the subject of intense research. In addition, they are also highly relevant for their medical aspects since defects in protein folding and chaperone function lead to protein aggregation. These protein aggregates are characteristic pathological markers for neurodegenerative diseases like prion diseases, Alzheimer's dementia or Chorea Huntington disease, and they are presumably responsible for the neuronal cell death.

2. Contents of the course

a) Theoretical part
Protein folding, function and mechanisms of molecular chaperones, protein folding defects, molecular basis of neurodegenerative diseases and aging, yeast and C. elegans as genetic model systems; biochemical methods for the analysis of protein-protein interactions: crosslinking techniques and fluorescence spectroscopy; detailed structural and functional insights into ribosomes and translation regulation.

b) Practical part
The practical part of this advanced course orients itself at our current research projects. Our major goal is to enhance our understanding of protein synthesis and folding in health and disease. Thus, the major topics of our research are

1. to illuminate the structural, functional and mechanistic principles of molecular chaperones with a particular emphasis on investigating the role of ribosome-associated chaperones that control protein folding and regulate translation;
2. to study cotranslational folding pathways of nascent polypeptides;
3. to investigate protein processing and quality control mechanisms that ensure that the newly made protein is either correctly modified and folded or rapidly degraded by proteolytic systems;
4. to understand the functions of ribosome-associated chaperones in aging and diseases related to protein misfolding.
c) Model organisms and range of methods
The questions raised above are worked on using three different model organisms: the bacterium *Escherichia coli* and the yeast *Saccharomyces cerevisiae* as well as the nematode *C. elegans*. For our work, we combine demanding genetic analyses of chaperone and ribosome mutants *in vivo* with protein analysis *in vitro*. This includes RNAi experiments in *C. elegans*, knockout mutations in *E. coli* and yeast and fluorescence microscopy analysis with all three model systems. Furthermore, state-of-the-art kinetic and mechanistic investigations of translation and chaperone-assisted protein folding *in vitro* are performed using translation systems, ribosome profiling, qPCR, fluorescence spectroscopy and crosslinking techniques.

3. State of knowledge of the participants
a) Compact course Molecular Microbiology;

b) Elementary knowledge in microbiology, biochemistry and molecular biology including all the techniques like protein purification methods, PCR, cloning, etc. is a prerequisite.

4. Literature

a) General
- Lubert Stryer "Biochemie"
- Michael T. Madigan, John M. Martinko und Thomas D. Brock "Mikrobiologie"
- Bruce Alberts, Alexander Johnson und Julian Lewis " Molekularbiologie der Zelle"
- Friedrich Lottspeich und Haralabos Zorbas "Bioanalytik"

b) Special


Preissler, S., et al. (2015) Not4-dependent translation repression is important for cellular protein homeostasis in yeast. EMBO J. 34, 1905-1924


Kirstein-Miles, et al. (2013) The nascent polypeptide-associated complex is a key regulator of proteostasis, EMBO J. 32, 1451-1468


Advanced Course „Human and Environmental Toxicology”

Date: 09.11.20 – 18.12.20

Location: Lab-1014, Level 10 M-Building, Universitätsstrasse 10, D-78457 Konstanz, Germany

Coordinators: Prof. Dr. Daniel Dietrich (Daniel.Dietrich@uni-konstanz.de)
Dr. Sascha Beneke (Sascha.Beneke@uni-konstanz.de)

1. Introduction

With a continuously growing knowledge about the limitation of our natural resources the needs were arising to assess comprehensively the risks of single individuals and communities from damages caused by an increasing population density, industrialisation and modernisation of the society. Particularly, of growing concern is the increasing number of ubiquitously distributed xenobiotics at low concentrations, mostly of anthropogenic origin, which potentially could be toxic for humans and animals. The xenobiotics are not only equally distributed in the environment, but can also be distributed and accumulated in various organisms including humans, e.g. via direct (water, drinking water) or indirect exposure (food chain). Primarily human and environmental toxicology focus on the acquisition, assessment (and at best in the future on prediction and prevention) of interactions between anthropogenic agents and the ecosystem including species/individual organisms and humans. In view of the large number of chemical agents, the complexity of the ecosystem and the rapidly changing living and eating habits of our society this goal seems to be difficult to achieve. Therefore, environmental toxicology is a multidisciplinary field of science that is not only concerned with the study of the harmful effects of various chemical, biological and physical agents on individual living organisms, but also considers aspects of environmental chemistry and ecology and put them in a common context. The major goal is the determination of the risk potential of specific substances, whether of natural (e.g. cyanobacterial toxins) or of anthropogenic (e.g. pharmaceuticals) origin, while considering also factors e.g. physicochemical characteristics and amount released, property and size of the affected environmental compartment, period and route of exposure of individual organisms and closely associated different substance effects. Furthermore, the research also encompasses developments of effects caused by global warming like the potential selection of temperature-tolerant toxin-producing cyanobacterial strains or resp. the invasion of toxic neobiota into the temperate climate zone along with the problems of toxin contamination of surface waters and drinking water.

Since humans, as part of the living environment, are primary organism to be protected from adverse effects incurred by exposure to toxic substances, the field of environmental toxicology cannot be separated from the medically oriented human toxicology. In order to address the many issues of environmental and human toxicology numerous research methods for application in the laboratory, but also model ecosystems and field studies have been developed.
2. Research topics

The research of the Human and environmental toxicology group focuses on

- environmental behaviour and toxicokinetics and dynamics of cyanobacterial toxins, e.g. microcystins or anabaenopeptolins, or marine biotoxins, e.g. ciguatoxins, on various organs, like liver, lungs, kidneys and the CNS
- nephrotoxic and cancerogenic effects of plant toxins, e.g. aristolochic acid, or mycotoxins, e.g. ochratoxin
- development of a suitable test-system for nephrotoxins in humans, with a special focus on physiological oxygen concentrations (PhysOx)
- Schwarzenbachtalsperre, New Zealand Laboratories (Field & Lab work)

3. Course

The participants will work under supervision on subprojects of current research work. One week prior to the beginning of the course an introductory lecture will take place. In the latter, participants will be informed about individual projects, the respective supervisors and the experimental methods. Additionally, all organisational details will be discussed (notification date on our home page https://www.biologie.uni-konstanz.de/dietrich/ and the information board of Fachbereich Biologie). During week 1 to 5 from 8.15 – 10.00 a.m. daily lectures and workshops with different speakers of the team will take place. Optionally, seminars with external speakers will amend the seminar schedule. During the first week a project plan will be worked out by the participants and presented at the end of the week to the group members. Literature seminars will take place on a regular basis with the aim to discuss methodical aspects and intensify the knowledge in the chosen research topic. The practical part of the project will be performed between week 2 and 5, finalised and the project results will be presented in week 6. At the end of the course each participant will submit a scientific protocol of his/her work in the style of a publication.

This course can be used as preparation for a future master thesis.

Theoretical part (lectures, seminars and workshops)

- Part A: laboratory safety, scientific writing and test documentation, statistics
- Part B: general toxicology, e.g. behaviour of xenobiotics in the organism (ADME), organ toxicology and pathology (liver, kidney, lung, nervous and hormone system), cancerogenesis, molecular toxicology
- Part C: environmental toxicology, transport and environmental behaviour of xenobiotics, aquatic toxicology, terrestrial toxicology, risk assessment of toxic substances
- Part D: „case studies“ of the field of environmental toxicology, applied toxicology, seminars on related scientific topics with speakers from different research groups and academic institutes

Experimental part (applied methodology)

- Analytics (HPLC, UV-VIS, Mass Spectrometry)
- Cell biology: stable cell lines, primary cells from various species and organs, cytotoxicity assays, cell proliferation analysis, transfection
- Protein biochemistry: Western blotting, ELISA, immunocytochemistry, FACS analyses, enzyme kinetics, cellular transport studies
- Molecular biology: DNA/RNA isolation from cells or tissue, PCR, real-timePCR, screening of a cDNA library
- Data evaluation and interpretation, statistics

For lab course participants of the VTK:
In order to pass this course, lab course participants need to fulfil the following requirements:

- regular participation in all lectures, including introductory project presentation (week 1), final presentation of the project results (week 6),
- power-point presentation of specific publications at the literature seminars
- practical work under supervision (week 1-6)
- continuous maintenance of a lab journal and timely delivery to the supervisor
- final presentation of course work as a power-point based talk at the end of the course (graded for Life Science students in accordance with study requirements)
- timely submission of a complete work report in English in manuscript form, compiled in accordance to the general rules for scientific writing and the guidance for authors provided at: https://www.journals.elsevier.com/chemico-biological-interactions

For students taking part only in lectures and not part of the VTK:
Participation in ALL lectures and seminars and a final written exam of 1 hour is mandatory in order to achieve the 5 ECTs.

Desirable state of knowledge of the participants
Prerequisite for a successful participation of this course are basic knowledge in “Molecular Toxicology” or “Disease Biology” (Prof. A. Bürkle), “In vitro Toxicology” (Prof. M. Leist), and “Environmental Toxicology” (Prof. D. Dietrich). Basic knowledge of statistics, profound expertise in using of computers, especially of current standard programs, like MS-Office, digital imaging and graphics. In particular, to allow experimentation with primary cell cultures, sufficient protection from hepatitis and tetanus via prior vaccination is mandatory.

4. Recommended literature


Project related literature:


Advanced Course "Environmental Genomics"

Coordinator: Prof. Dr. Laura Epp

General research topic
Current advances in molecular genetic techniques offer the possibility to investigate present and past biodiversity using DNA extracted directly from environmental samples, such as water or sediments. This environmental DNA (eDNA) is shed into the environment by all organisms, both microbial and macrobial, and it can be used to identify species and sub-specific variation. We can thus analyse diversity patterns in space and through time, both at the level of species composition of biotic communities and within single species. We apply these techniques to study questions of ecosystem history and environmental change.

Structure and objectives of the course
The course is structured around small research projects related to ongoing work in our group, in which you will learn the practical steps of environmental DNA analyses, from sampling through wet-lab methods to bioinformatics. In accompanying lectures and workshops, you will be introduced to the underlying theoretical principles of environmental DNA analyses and will learn analytical skills as well as scientific writing and project planning. In a literature seminar you will present and discuss papers highlighting current applications of environmental DNA in ecology and paleoecology.

Objectives
In this course you will
- gain a thorough current understanding and practical experience of the application and uses of environmental DNA in ecological research
- learn how to acquire and analyze different types of eDNA data by designing your own reactions for eDNA (bioinformatically and in the lab)
- acquire skills in designing and conducting a research project
- gain an understanding of the scales and causes of ecosystem changes at different timescales (centennial, millenial)
- expand your presentation skills
**Techniques and theoretical concepts covered**

- sampling and extraction of environmental DNA.
- specificities of working with ancient and degraded DNA.
- bioinformatic design of reactions to trace target organisms in water and sediments.
- wet-lab evaluation and application of these reactions: (quantitative) PCR and DNA-metabarcoding.
- bioinformatic analyses of NGS sequencing data from environmental samples
- taxonomic assignments of DNA sequences using reference databases

**Literature**

**Book**

**Articles**


1. Introduction

Our group is interested in the intracellular processing of antigens and the presentation of the antigens to cytotoxic T-lymphocytes. Protein antigens are degraded in cells by a large protease complex, the proteasome. The generated peptides are bound by MHC class I molecules, transported to the cell surface and presented to the antigen receptor of the T-killer cells. We determine how the subunit composition of proteasomes affects the immune response of the T cells against viruses and tumors. Recently, we have discovered a new function of a subtype of the proteasome in immune cells, the immunoproteasome, in autoimmune diseases. The mechanistic basis and therapeutic implications of this finding will be investigated. Please note that some of the participants will do their experimental work at the Biotechnology Institute Thurgau in Kreuzlingen, Switzerland (www.bitg.ch), which is 6 km away from the Chair for Immunology on floor P11 of the Konstanz University Campus.

Our current work focus:

a) The role of proteasome regulator PA28α/β and the interferon gamma induced subunits of the 20S immunoproteasome in the immune response against murine lymphocytic choriomeningitis virus and other pathogens.

b) The regulation of maturation and migration of dendritic cells through pro-inflammatory cytokines.

c) The function of a ubiquitin-like protein called FAT10, which is induced by interferon gamma and is encoded in the MHC.

d) The function of the immunoproteasome in the pathogenesis of autoimmunity and cancer.

2. Course schedule

a) Theoretical part

Week 1 and 2 daily from 9 – 11 o’clock:
lectures on new developments in Immunology with main focus on the current research topics
afterwards – work in the lab

Week 3 to 5 daily from 9 – 11 o’clock:
presentation of recent top publications in immunology by the students.
The presentations will be held in English.
afterwards – work in the lab

Week 6 Oral presentation of the students’ data.

b) Experimental part and methods

Every student is working with a scientist or PhD-student on his/her project. The experimental scheduling is adapted to our current scientific research projects and the ongoing experiments. We use methods of molecular biology (plasmid preparation, restriction analysis, real time RT-PCR, molecular cloning), of protein chemistry (immuno-
precipitation, Western blot, isolation of proteins with various chromatographic methods), and immunological methods (ELISA, ELISPOT, flow cytometry, proliferation assays, adoptive transfer, cytolytic assays, immunofluorescence microscopy) and for some experiments work with mice.

c) Requirements

To pass the course (for biological science students: obtain a “Schein”; for life science students: obtain a mark) the following requirements need to be met:
Participation in the lectures, presentation of the project results, power point presentation of a recent immunological publication at the literature seminar, submission of a comprehensive work protocol in English language formatted like a research article in The Journal of Immunology (http://jimmunol.org/misc/ifora.shtml).

3. Qualification of course members

Students need to have attended the lectures of Immunology in the 4th semester at Konstanz University and must have passed the associated exam. Equivalent qualifications of students from outside Universities are accepted. The content of the lectures must be refreshed using the script and the textbook “Immunobiology” by Charles Janeway et al. before the start of the course. Basic knowledge in biochemistry, cell biology, molecular biology and good command of English is required. We expect a higher-than-average interest in Immunology and immunological research projects.

4. Literature


Advanced Course “Applied Bioinformatics for Studying Health and Disease”

Coordinator: Prof. Dr. Andreas Gruber

**Topic of the course**

Understanding the molecular basis of healthy cells enables the identification of alterations that are key to human disease. Molecular cell biology can be studied on a systems scale by sequencing whole genomes and/or measuring the activity of thousands of genes in parallel, both of which can be achieved using next-generation sequencing (NGS). Over the past decade, NGS technologies significantly advanced and became broadly available for basic research and clinical diagnostics. However, even though the availability of NGS datasets increases on a fast pace, the information content that NGS datasets harbour is far from being exploited. In recent years, a large toolbox of data science approaches has been developed. These tools make it now possible to study many aspects of molecular cell biology, and have great potential to drastically improve our understanding of healthy cells, but also of molecular dysregulations underlying human disease.

In our research we analyse high-throughput sequencing data by applying available as well as in-house developed, machine learning-based data science approaches to study healthy and diseased cellular states in human (Homo sapiens) and mouse (Mus musculus). In particular, we are interested in gene expression regulation in the context of:

(i) basic cellular processes (e.g. adhesion, transcription, splicing, 3’ end processing)
(ii) the immune system (e.g. immune cell function, identity, activation and interactions)
(iii) virus-host cell interactions (e.g. host cell response, host factors utilized by viruses)
(iv) cancer development, progression and therapy (e.g. mutational patterns, transcript isoform expression programs, immune escape)

**Aims and contents of the course**

This course aims to provide you with the theoretical background and practical fundamentals of NGS data analysis. In lectures and seminars, you will gather theoretical knowledge on high-throughput sequencing technologies and data science tools for the analysis of large-scale NGS datasets. For the practical hands-on sessions, you will get assigned a small research project from one of the above mentioned topics. In this course you will:

1. learn to **search databases** for reference genomes, gene annotations, and datasets
2. understand **NGS data** and get skilled in data **quality control**
3. **map NGS data** to a reference genome (human or mouse)
4. learn how to **infer global gene expression** from NGS data
5. understand the concepts behind identifying **differential expressed genes**
6. gain data science skills allowing you to investigate **gene expression at systems scale** (e.g. by applying **clustering** and **dimensionality reduction** algorithms)
7. identify **transcriptional regulators** that explain global changes in isoform expression
8. read, understand and present **bioinformatics literature**
9. relate your data analysis results to the **current scientific knowledge / publications**
10. design a research project, follow-up analyses and validation experiments
11. document, write-up and present your analysis and research results, using FAIR (Findable, Accessible, Interoperable, Reusable) data principles, which will be introduced, discussed and applied throughout the course.

Requirements to pass the course

All of the requirements mentioned below can be completed during the course:
- Attendance and active participation in all the theoretical lectures, seminars and practical sessions.
- Presentation and discussion of an assigned scientific publication (literature seminar).
- Submission of a scientific report and presentation of the research project results.

Qualification / Required pre-knowledge

It is expected, that students have basic cell biology knowledge and an interest in the molecular foundations of health and disease. Before every practical hands-on course the required background knowledge will be presented and extensively discussed within theoretical sessions (lectures and seminars). Importantly, the practical hands-on sessions will build up from the very basics and thus no prior programming or data science skills are required. However, to be qualified for the course students should be interested in gaining data science skills and be willing to touch base with data analysis challenges. In the course we will be using bash commands (Linux) and the programming languages R and Python. However, the overarching goal of the performed analyses is cell biology research, ultimately aiming to extend our knowledge about the molecular foundations of health and disease.

Further reading

Reviews on Relevant Molecular Cell Biology Topics

Review on NGS Data Generation and Analysis

Example Data Science Tools for Analysing NGS Data
Advanced Course "Cell Biology – Cell Adhesion and Signal Transduction"

Coordinator: Prof. Dr. Christof R. Hauck

1. Background

Cellular adhesion receptors are critical for many cellular processes by providing stable connections between cells and the extracellular matrix. Cellular adhesion receptors also mediate cell-cell interactions, together allowing the formation of tissues and organs in multicellular animals. Besides their mechanical support function, adhesion receptors of the integrin, cadherin or immunoglobulin protein families help to organize the intracellular cytoskeleton and contribute to signal transduction processes that guide cell proliferation, differentiation and survival, as well as cell motility. Moreover, the surface exposed nature of cell adhesion receptors as well as their functional connection to the cytoskeleton makes these proteins preferred targets for viral and bacterial pathogens.

In the frame of this advanced laboratory course, we try to answer some pertinent questions in the field of cell adhesion receptors. In particular, we will focus on integrins and the regulation of their function as well as on immunoglobulin-related cell adhesion molecules of the CEACAM family and their role as receptors for pathogenic bacteria.

In this context, we will employ molecular biological methods to generate recombinant DNA and proteins, which will be used for plasmid transfection, viral or protein transduction, and RNAi- or CRISPR/Cas-mediated knock-down of protein expression. Genetically manipulated cells will be employed in functional assays of cell adhesion, cell migration, cytoskeletal organization, or endocytosis/phagocytosis and will be further investigated by advanced microscopy techniques or flow cytometry (FACS analysis). As protein-protein interactions are a prominent characteristic of signalling cascades in eukaryotic cells, we apply a diverse set of methods (pull-down analyses, co-immunoprecipitation, FRET measurements, protein domain microarrays) to identify and monitor the regulated association of proteins. Finally, signal transduction pathways often regulate characteristic gene expression events, which will be studied by quantitative real-time PCR and luciferase-based promoter assays.

2. Content of the Advanced Laboratory Course

A) Theoretical Part: Lectures and Seminar

The lecture part is spanning the first four weeks of the course. In the first part, the lectures cover the following areas of cell biology: adhesion molecules, integrins, IgCAMs; focal adhesions, protein phosphorylation: kinases/ phosphatases, adapter proteins/ protein-protein-interaction domains/ SH3-domains/ SH2- domains / ITAMs/ITIMs, lipid phosphorylation: kinases/ phosphatases, endocytosis – autophagocytosis, lipid rafts, vesicle trafficking, dynamics of the actin cytoskeleton, regulation of cell migration, phagocytosis, innate immunity, cellular microbiology. Selected pathogenic bacteria will be

In the second part of the lecture series, common **experimental strategies**, and the **principles, application and pitfalls of** the used **methodology** will be discussed, in particular we talk about cell culture, hybridoma cells, monoclonal antibodies, manipulation of cells – transfection, transduction, RNA-interference (RNAi), microRNAs, siRNA, shRNA, generation of transgenic and knock-out mice, genome editing strategies, fluorescence labeling and detection, flow cytometry, fluorescence spectroscopy; "Microscopy": electron microscopy, advanced fluorescence microscopy: confocal microscopy, TIRF, FRAP, FRET, FLIM; protein detection: epitope-tagging, GFP-fusion, Western Blot, autoradiography, detection of protein-protein-interactions: Far-Western-Blot, GST-pull-down, Co-IP, protein-arrays identification of novel protein-protein-interactions: yeast-2-hybrid, QUICK; affinity purification of proteins: GST, His-tag, antibodies.

In the last two weeks of the course, a literature seminar is held, where current publications and breakthrough findings in the above mentioned areas will be presented and discussed in detail. Each student presents one original paper.

**B) Experimental Part**

Individual projects will be conducted alongside existing lines of investigation in the field of cell adhesion receptors and address the following topics:

- CEACAMs & Neisseria, Integrins & staphylococci, Regulation of cell adhesion, Advanced Methodology in Light & Electron Microscopy
- Examples of recent projects: CEACAM-initiated signalling in granulocytes; The adapter molecule Nck is involved in phagocytosis of *Neisseria gonorrhoeae*; CRISPR/Cas-mediated knock-out of alpha-actinin; From human CEA to chimpanzee CEA via site-directed mutagenesis; Role of Vinculin in the Internalization of *Staphylococcus aureus*; Influence of CD105 on subcellular localization of zyxin; Role of Focal Adhesion Kinase (FAK) in cell migration

**3. Requirements**

The lectures Cell Biology I and II, Biochemistry II, and Immunology or equivalents to these lectures must have been followed and passed. A specific introduction into laboratory safety is mandatory and will be given on the first day of the course.

To pass the course (for biological science students: obtain a “Schein”; for life science students: obtain a mark) the following requirements need to be met:

- Active participation in the lectures, power point presentation in the literature seminar, research project and presentation of the project results in the form of a scientific poster.

**4. Literature**

Pollard/Earnshaw „Cell Biology“ 2nd edition (Sauners/Elsevier)

Easy Reading edition by Spektrum Akademischer Verlag, Berlin – Heidelberg

Signatur der UB Konstanz: lbs 670/p65b
Advanced Course "Physiology and Biochemistry of Plants"

Coordinator: Prof. Dr. Erika Isono

For the lab work, we offer small projects from our ongoing research projects that use diverse methods in molecular biology, protein biochemistry and cell biology. Projects will be presented on the first day of the course and can be chosen by the participants. Lectures will focus on state-of-the-art techniques as well as current topics in the research field of ubiquitin biology, endocytosis and autophagy and are complemented with a journal club and final presentations held by participants.

Keywords: ubiquitin, membrane trafficking, endocytosis, autophagy, posttranslational modifications

Methods and Techniques:
Molecular biology: Isolation of RNA and DNA, PCR, qRT-PCR, molecular cloning (overexpression constructs, epitope- or GFP-tagged proteins).
Protein biochemistry: Recombinant protein expression and purification, in vitro binding assays, MicroScale Thermophoresis, analysis of posttranslational modifications, in vitro DUB assays, SDS-PAGE and Western blotting, yeast two-hybrid, clathrin coated vesicle (CCV) isolation.
Imaging: Epifluorescence and confocal microscopy using Arabidopsis seedlings of Arabidopsis cell cultures. Depending on the project, electron microscopic analysis will be applied.
Genetics: Isolation and characterisation of knockout and knockdown mutants.

Projects:

Figure 1: Ubiquitin-dependent membrane trafficking. Membrane proteins are endocytosed via clathrin coated vesicles CCVs) upon ubiquitination and transported via the endosomal trafficking pathway to the vacuole for degradation. Proteins for selective autophagic degradation are similarly transported to the vacuole by autophagosomes upon ubiquitination. The regulation of protein stability is crucial for almost all physiological pathways.
Background: Plasma membrane receptors and transporters play crucial roles in the coordination of extracellular stimuli and intracellular responses that enable plants to react readily to environmental changes and stress. Regulation of the abundance of plasma membrane receptors by endocytosis-dependent protein degradation in the vacuole is an important regulatory mechanism in a variety of signaling pathways such as phytohormone signaling and biotic- and abiotic stress responses.

Regulation of ubiquitination in intracellular membrane trafficking of plants

We aim to understand the molecular mechanisms by which ubiquitin is regulating protein degradation in the model plant Arabidopsis thaliana with a special focus on endocytosis and the subsequent protein transport to the vacuole (Figure 1). Ubiquitination is a post-translational process in which ubiquitin, a highly conserved small protein of 76 aa, is covalently attached to substrate proteins and is, among others, a signal for selective protein degradation. Depending on the modification type (mono-ubiquitination, K48, K63 and other linkages), ubiquitination can serve as signals in various cellular processes. Since many of these target proteins are key regulatory factors of different signaling pathways, it is essential that the processes of ubiquitin conjugation and deconjugation are strictly regulated.

Function of deubiquitinating enzymes in plants

The conjugation of ubiquitin molecules to its target proteins is a process that is mediated by the activity of E1, E2 and E3, in which the combination of the E2 and E3 enzymes usually defines the ubiquitin chain-type to be conjugated as well as substrate specificity. Deubiquitination, on the other hand, is mostly carried out by a single DUB (Figure 2). Though the ubiquitination machinery plays a key role in determining target protein stability, DUBs can also influence target protein fate by removing the ubiquitin signals from the protein. In most of the cases the interaction of the DUB with the conjugated ubiquitin chain, rather than with the target protein itself, is sufficient for target deubiquitination. The spatio-temporal regulation of DUBs is therefore crucial for deubiquitination of the correct target proteins. Our aim is to characterize Arabidopsis DUBs that are involved in the regulation of protein stability and to understand their physiological functions.

![Figure 2: Ubiquitination is a reversible process.](image_url)

A protein, targeted for degradation, is labeled by ubiquitin through the enzyme cascade of E1, E2 and E3. Deubiquitinating enzymes (DUBs) counteract this enzyme cascade and remove the ubiquitin from the target protein.
Introduction
The aim of our research is to unravel how neural circuits enable animals to sense their environment, how such information is processed in the brain and used to guide behavior, and how an animal's internal state modulates the underlying network dynamics. To this end, we study how animals make decisions in different contexts and states, how they learn and remember, and how they interact when in a group.

We are generally driven by the idea that biological systems, in their beautiful diversity and complexity, follow relatively simple principles that are commonly shared across species. To explore these common principles, we use a variety of model organisms, including larval zebrafish, locusts, bees, ants, cockroaches, adult flies, and fly larvae. Each one of these model organisms has its specific experimental advantage or shows a particularly interesting behavior:

- **Larval zebrafish** are tiny and almost completely transparent vertebrates, making it easy to use functional imaging techniques to characterize the activity of the entire brain at cellular resolution, while animals can still make behavioral decisions. Larval zebrafish are genetically tractable, allowing us to manipulate circuit function and test its effect on behavior.
- **Locusts** show complex group dynamics, they often march or fly in huge groups, which can be mimicked in a laboratory setting. Using electrophysiological recordings and imaging techniques we can ask how such different behavioral states arise and how this affects sensory processing.
- **Bees** are masters in olfactory processing, spatial memory, and communication, and can make complex decisions as a collective. It is possible to use imaging and electrophysiological techniques to dissect the combinatorial code in the olfactory system and explore how memories are stored. In behavioral experiments, the division of labor and the organization of the colony can be explored.
- **Ants** are highly social insects and can collectively shape their environment by cutting grass and leaves, and by keeping their environment tidy. Through behavioral experiments,
immunohistochemical staining methods, as well as mass spectrometry, we explore how nervous system activity changes as a function of the animal’s state.

- **Cockroaches** have a very fine sense of odor and actively sample their environment using their long antennae. Through behavioral quantification and electrophysical recordings, we aim to understand their behavioral strategies in odor plume detection and how this information is represented on the level of the brain.

- **Fruit flies** perform sophisticated navigation behaviors towards olfactory or visual cues, which are also modulated by their internal state. Furthermore, they are able to associate rewarding and punishing events with different contextual stimuli, allowing them to adapt their behavior for future behavioral decisions. Using the most powerful genetic toolkit available across all our model organisms, we can dissect the neural circuits underlying all these behaviors on the level of single-cell types. Additionally, we can investigate how genetic modulations affect the activity of other cells in the brain by functional imaging.

**Contents of the Course**

Students will join one of our currently active research projects, using one of our animal models. Working closely together within our scientific community, we will provide students with hands-on exposure in state-of-the-art experimental techniques, including high-throughput behavioral tracking, two-photon functional calcium-Imaging, electrophysiology, mass spectrometry, immunohistochemistry, molecular biology, and computational modeling.

The project work includes the development of a specific research question, literature research, planning of experimental design, experimental execution, data acquisition, and data analysis. The project ends with a detailed protocol in the form of a manuscript and a final presentation of results in the form of a talk.

The course is accompanied by lectures covering basics in Behavioral Neuroscience and general experimental techniques. Moreover, invited speakers give students the opportunity to learn about ongoing research in the field outside our department. In addition, we will hold a paper seminar where supervisors introduce their own research topic and where we discuss recent publications related to our projects. This will happen during a retreat in the Alps on one of the first weekends during the course.

Lectures, project completion, as well as seminar attendance, are mandatory parts of the course. This course is held in English only.

**Interested students should contact one of our principal investigators 2–4 weeks prior to the course to discuss possible research projects.**

**Recommended reading material**


Advanced Course "Global change ecology and plants"

Coordinator: Prof. Dr. Mark van Kleunen

1. Introduction
We are living in the *Anthropocene*, a period of unprecedented rapid environmental change. Human actions are driving changes in climate, the disappearance and fragmentation of natural habitats, and the introduction of exotic species to nearly every region of the world. These changes impose a challenge to many organisms, and opportunities to others. However, the exact ecological and evolutionary consequences of global change, and the impacts on ecosystem functions and services (e.g. supply of food and clean water) are still poorly understood.

A few impressions of our research. (a) The global flows of naturalized exotic plants, (b) our global-warming simulation facility, (c) experimental manipulation of nutrient availability.

We are interested in the basic questions of how phenotypic variation in functional traits is shaped by environmental and genetic variation, and how these traits interact with extrinsic factors to determine the success of species - plants in particular. As ecology and evolution are intrinsically related, we also address evolutionary questions. The approaches that we use include experiments in greenhouse and garden as well as field studies, but we also perform global syntheses of available knowledge through database studies and meta-analyses of published research.
2. Objectives
You will learn the “what” and “how” of Global Change Biology and Plant Ecology:

- What are the major…
  - drivers and impacts of global environmental change.
  - questions in global-change and plant ecology.
  - methods and approaches in plant (evolutionary) ecology.

- How to:
  - test hypotheses in ecology and evolution.
  - design, set-up, and run experiments.
  - analyse the data that you collect.
  - present your results (poster presentation, oral presentation, paper).

3. Contents of the course
The course consists of a combination of lectures, practicals, workshops, seminars and excursions. In the lectures, you will learn the major theories in global-change and plant ecology. In the practicals, you will learn the methods that we use. In the workshops, you will learn important skills, such as experimental design, statistical analysis, scientific writing and how to make a poster. In the seminars, you will present and discuss recent publications. During a one-day excursion to the mountains, you will learn about alpine ecology and take inspiration for a research proposal, and during another excursion you will gain insights in managing a nature reserve. In a small group, you will design and run your own research project, during which the acquired methods, skills and knowledge will be put into practice. Overall, you will obtain experience in all aspects of scientific research – from observing the natural world to presenting your completed research to colleagues.

4. Requirements and passing the course
Requirements are basic knowledge of and a keen interest in ecology and evolution. To pass the course, you have to actively participate, present and discuss papers and your project results, and write a paper on your research project.

For more information on our group, visit our webpage (http://cms.uni-konstanz.de/vkleunen/) or contact mark.vankleunen@uni-konstanz.de.
Advanced Course "Physiology, Ecology and Molecular Biology of Algae"

Coordinator: Prof. Dr. Peter G. Kroth

Algae in their variety of forms, colors and genetic constitutions are fascinating organisms that contribute considerably to life in this planet. We therefore are working on physiological, cellular, molecular and ecological aspects of diatoms to increase our understanding of their molecular and physiological functions. The current projects include photoreceptors, regulation of photosynthesis and photoprotection, the metabolism of storage carbohydrates, genomic aspects, biotechnological issues, and the role of diatoms in biofilms in Lake Constance.

**Genetic methods**: Cloning in *E. coli*, Transformation of diatoms (Particle Gun, conjugation), Real-Time-qPCR, RNA-Seq, Genome editing of algae via TALEN and CRISPR, expression von GFP fusion proteins, Northern blots, Southern blots, yeast-1-hybrid analyses.

**Biochemical methods**: Isolation of organelles, isolation of proteins, Western Blots, heterologous expression and purification of proteins in *E.coli*, SDS gel electrophoresis, 2D-electrophoresis, centrifugation, gel filtration, HPLC analyses of pigments, fluorescence quantification of lipids, enzymatic quantification of carbohydrates, extraction and characterization of signal molecules.

**Further methods**: fluorescence microscopy and confocal laser-scanning microscopy, PAM fluorometry, steady-state absorption and (77K and room temperature) fluorescence spectroscopy, particle- and fluorescence based cell counting, biofilm growth chambers, cell cultivation in bioreactors.

Storage Compounds in Diatoms

Chrysolaminarin is the main storage compound in diatoms, a glucan consisting of linear 1,3-β-chains with 1,6-β-branches. In diatoms, chrysolaminarin is stored in intracellular vacuoles in a non-crystalline form. The biosynthetic pathway of chrysolaminarin in diatoms as well as the involved enzymes so far are poorly investigated. Therefore, we aimed at studying this pathway in the diatom model system *Phaeodactylum tricornutum*. We screened the respective genome and identified genes encoding enzymes that are potentially involved in chrysolaminarin synthesis or modification, including UDP glucose pyrophosphorylases, a β-glucan synthase and β-1,6-transglycosylases. By expression of GFP fusion proteins in *P. tricornutum*, we determined the respective intracellular localizations of the proteins. We also investigated the functionality of the glucan synthase and the putative transglycosylases from *P. tricornutum*, by applying gene silencing techniques or by complementation of transglycosylase-deficient yeast strains. Silencing of the glucan synthase yielded a number of phenotypic cellular changes including reduced growth, a higher NPQ and a changed thylakoid morphology. Phylogenetic analyses finally revealed that these proteins are conserved between the Stramenopiles, a taxonomic group including diatom, brown algae and non-photosynthetic Oomycetes.
Photoprotection in Diatoms

Diatoms in their natural habitats need to cope with rapidly changing environmental conditions. One of these factors is light intensity. While the photosynthetic apparatus of diatoms is optimized to harvest as much light as possible under lower light intensities, it needs to be shut off during high light exposure, in order to prevent massive photo-oxidative damage. This is achieved via a light intensity dependent rapid and reversible mechanism called NPQ (Non-photochemical fluorescence Quenching). NPQ needs so called Lhcx proteins whose function is just becoming to be revealed. We are knocking out these Lhcx proteins and study their impact on the NPQ mechanism via PAM-fluorometry. We also mutate peptide motifs and single amino acids of Lhcx proteins hypothesized to be mandatory for NPQ (Fig. 3). Furthermore, we investigate the impact of a functional NPQ on cellular fitness via competition experiments in collaboration with the FlowKon facility.

Fig. 3: Impact of Tryptophan (W) 133 on NPQ capacity of Lhcx1 in P. tricornutum. Left: W 133 (indicated with a red arrow) in Lhcx1 is supposed to bind a specific pigment essential for NPQ (pink). Right: When mutating this W133 to a methionine, NPQ capacity is strongly reduced (red trace) compared to the wild type. The white box indicates a period of high light exposure, while the grey box indicates low light.

Light signaling in diatoms

Light is an essential abiotic factor, as it is the prerequisite of photosynthesis and hence photoautotrophy. Light is varying remarkably in colour and intensity depending on the specific aquatic habitat. E.g., in the open ocean the water layers are rather stable and hence a diatom experiences a light environment that follows the course of the sun and the cloudiness, and light colour changes towards blue the deeper the alga is placed in the water column. However, in coastal...
and estuary regions, light intensity changes within minutes massively, and light penetrating the water is enriched in the green and red spectral parts. Diatoms need to adjust their metabolism to these changing environments. They do this by means of direct light signaling via photoreceptors (e.g. aureochromes, see below) and by indirect light signaling via signals generated in the chloroplast - so called retrograde signaling. Regarding retrograde signaling, we investigate the role of the redox state of the plastoquinone pool on changes in the nuclear transcriptome by pharmaceutical manipulations, gene editing, and RNA-Seq/qPCR.

**Fig. 4:** Model how light influences nuclear gene expression via changes in the plastid redox state. Light influences photosynthesis. The ratio photosynthetic light reaction/Calvin cycle determines the redox state of the plastoquinone pool (PQ). A reduced PQ-pool can emit a signal across the four membrane plastid envelope into the nucleus and influences expression of specific genes, such as *Lhcx*. The corresponding proteins are co-translationally inserted into the endoplasmatic reticulum (ER), from where they are targeted to the thylakoid membrane, where they confer photoprotection, thus eventually relieving electron pressure and hence oxidizing the PQ-pool.

**Aureochromes, new and very fast blue light photoreceptors in algae**

Recently, a new type of photoreceptor has been discovered, which is only found in stramenopile algae. Aureochromes are unique blue light receptors as they simultaneously represent transcription factors, thus light driven gene switches. We have generated TALEN-based (Transcription activator-like effector nucleases) aureochrome deletion mutants. Characterization of Aureochrome 1a knockout cell lines indicates non-overlapping functions, which cannot be compensated for by the other isoforms. Moreover, this Aureochrome 1a seems to be one of the most effective master switches of gene regulation in the whole eukaryotic kingdom. We are using transcriptomic data as well as cell biology tools to identify interaction partners and transcription factors to understand how light is converted into a cellular response.

**Fig. 5:** While plants use phototropins as photoreceptors, diatoms have aureochromes. Both photoreceptors contain LOV domains (Light, oxygen, voltage), however, while phototropins initiate signaling cascades via a kinase, aureochromes are transcription factors that can start transcription of a target gene immediately.
Annotation of Diatom Genomes and Development of Molecular Tools for Algae

Meanwhile a number of diatom genomes have been published, and our group is involved in the annotation process of several genome and metagenome projects on eukaryotic algae. The analysis of the genome uncovered a series of surprises. For example, many of the Calvin Cycle enzymes can be found in the genome in multiple copy numbers. We are also involved in developing a number of molecular tools for diatoms including gene silencing, complementation, and genome editing via TALENs and CRISPR/Cas9.

Characterization and relevance of diatoms in biofilms of Lake Constance

Phototrophic, epilithic biofilms are a typical feature of aquatic ecosystems. In order to study interactions between diatoms and bacteria in biofilms, we have isolated and identified different diatoms and associated satellite bacteria from Lake Constance. Interestingly, purified diatom cultures showed significant differences with respect to growth and biofilm formation when compared to the corresponding xenic cultures. The diatom *Achnanthidium minutissimum* forms capsule-like structures in the presence of an isolated bacterial strain, but not in axenic state. Interestingly, formation of capsules can be induced by adding substances secreted by the satellite bacteria. We recently sequenced the genome of this bacterium (Dow et al., 2020). Transcriptome studies show that *P. tricornutum* strongly responds to a presence of bacteria. We furthermore try to identify diatom receptors that identify bacterial signalling substances based on leucine-rich repeat (LRR) structures.

![Identification of *A. minutissimum* capsules (asterisks) by successive observation of cell clusters by first bright-field and then scanning electron microscopy of a xenic biofilm (scale bars: 5 µm).](image)

**Fig. 6:** Identification of *A. minutissimum* capsules (asterisks) by successive observation of cell clusters by first bright-field and then scanning electron microscopy of a xenic biofilm (scale bars: 5 µm). (A) Bright-field micrograph of crystal violet (CV) stained, 31 days old culture. Encapsulated cells (asterisks) are strongly stained, while weak staining indicates few extracellular polymeric substances (EPS) on the frustule surfaces. (B) Scanning electron micrograph of the same cell cluster. Encapsulated cells (asterisks) are surrounded by an opaque material. Frustule pores are visible on cells that did not possess a capsule in the hydrated biofilm. Note also the unequal distribution of bacteria cells on capsules versus non-encapsulated frustules (Leinweber and Kroth, 2015).

Dinotoms are peculiar dinoflagellates using diatoms as endosymbionts

Dinotoms are dinoflagellates, unicellular eukaryotes, that have tertiary plastids derived from diatoms. They are excellent model organisms for studying the early evolutionary stages of plastids. Dinotom plastids are in evolutionary intermediate stages, which all other phototrophs had already passed through long time ago: all diatom organelles are still preserved within dinotoms, not just the plastids. Each dinotom species contains different species of diatoms, and these diatoms show different evolutionary stages from temporarily-maintained kleptoplastids to permanently-maintained endosymbionts (Yamada et al., 2019). Studying these host/endosymbionts with molecular tools allows insights into the very first processes of organelle establishment.
Fig. 7: A scheme of diatom nuclear dynamics in three dinotoms, *Durinska baltica*, *D*. *kwazulunatalensis* and *D. capensis*. (from Yamada et al., 2019)

If you should be interested in algae and diatoms, you can find some of our recent publications here:


Advanced Course "Novel in vitro methods in pharmacology and toxicology"

Koordinator: Prof. Dr. M. Leist

Introduction:
We use predominantly human cell cultures to examine disease processes and toxicity in the nervous system. For models of developmental neurotoxicity, we use stem cells that differentiate to neural cells (neural stem cells, neurons, glial cells). We use different approaches to characterize the developmental changes that the cells undertake over time, and new methods for better control and characterization of the differentiation are being developed. We use such models to study toxicity of drugs and environmental compounds (in particular pesticides). Thus, the course program will involve stem cell biology, cellular metabolism and signal transduction, neurobiology, epigenetic changes of developing cells and of cells exposed to stress, as well as characterizations of toxicity and cell death. This also involves complex interactions of various cell types. Some analyses are performed on systems wide (e.g. whole transcriptome, metabolome) levels to get a comprehensive overview of cellular responses on a systems biology level. This also involves characterization of larger sets of chemicals in part with several European partner laboratories. We are particularly interested in characterizing stress response pathways in cells, related to oxidative, mitochondrial and proteotoxic stress (as observed in Parkinson’s disease).

Our current research interest, and therefore also the projects offered during the course are:

2. Cocultures of glial cells and neurons (also in 3D) to better study toxic processes e.g. of pesticides or proteasome inhibitors.
3. Examination of the pathways that determine the generation of glial cells in the brain. Modulation of gliogenesis, and de-differentiation back to stem cells.
4. Differentiation of embryonic stem cells to neuronal precursor cells and mature neurons: examination of transcriptional changes associated with differentiation; examination of differentiation processes sensitive to certain toxicants.
5. Examination of functional properties of "young neurons", such as the migration of neural crest cells or the neurite growth of neural precursors as targets of toxicity.
6. Study of calcium regulation and toxicity mechanisms on human peripheral neurons triggered by natural toxins from bacteria and algae.
7. Interaction of cells with complex matrices synthesized in-house.
8. Study of neuronal electrical networks

The projects use cell culture technology, fluorescent staining and imaging technologies (high content automated imaging, pattern recognition and quantitative microscopy), FACS analysis, RT-PCR and SeaHorse mitochondrial analysis methods. Some involve lentiviral vector construction, Western blotting, chromatin precipitation, and several projects are linked to our interest in transcriptome and metabolome changes. This implies also data mining, statistics and visualization approaches.
Course theory:
In the lecture part, a lot of cross-sectional topics from biochemistry, pharmacology, cell biology, immunology and molecular biology will be covered as they form the basis for cell culture models. We will cover many internationally-used toxicological test systems and explain the 3R (reduce, replace, refine) principle of moderate and rational animal protection, and its scientific basis. A particular focus will be our own research interest, i.e. human cell-based models for the pharmacology of neurodegenerative diseases (Parkinson, Alzheimer Schizophrenia), and models that would predict chronic and developmental neurotoxicity in humans.

The course introduces the drug discovery processes and selected aspects of neuropharmacology and neuropathology. Some pre-knowledge in pharmacology and toxicology is STRONGLY advisable, as alternative methods cut across these disciplines in many examples. The lectures will cover the whole range of 3R methods, but they focus particularly on specific scientific interests of our group. The lectures will be in English, if foreigners are present. Some lectures will be given by international guest researchers in forms of seminars or a minisymposium. In week 4 and 5 of the course, selected publications from the scientific literature will be presented by students (English presentations). The discussion will clarify methodic aspects, and the relation of the chosen topic to actual research problems. Students are guided to critically judge third party data. Ethical aspects and the presentation style will also be addressed.

Literature: all material will be provided during the lectures. Some introductory literature on alternative methods and on the use of embryonic stem cells can be downloaded from our website: [http://cms.uni-konstanz.de/leist/research/](http://cms.uni-konstanz.de/leist/research/)

Requirements:
The knowledge covered by the lecture series Human Biology, Pharmacology and Toxicology I, and Biochemistry II is required. Basic knowledge of immunology would be desirable. The status of general knowledge and the capability to perform simple lab routine calculations may be tested at the beginning of the course.

Course projects:
Projects are within the areas of nervous system degeneration and re-generation, including pathobiochemical mechanisms implicated in chronic neurodegenerative disease and neurotoxicity. They will follow the research projects run at that time in the research group (see above, also for techniques used). Knowledge of mechanisms will be translated into the development of improved in vitro test methods and potential treatment strategies of disease. The results of the student projects will be presented and discussed in the final week.

Students following only the theoretical part of the course will investigate a new or important technology, and present it to others in form of a poster

Exam:
To pass the course (for biological science students: obtain a “Schein”; for life science students: obtain a mark) the following requirements need to be met:

Attendance and active participation in the lectures; research project and presentation of its results; power point presentation at the literature seminar and subsequent discussion of the paper and its background (!). In case of good progress in the lab project, a poster on the results can be presented at the end of the course instead of the protocol preparation. Technology posters will be presented by ‘theory students’ as main assignment. A test of theoretical knowledge may be performed during the course, if performance cannot be judged otherwise.
In order to understand living systems, it is essential to understand the function of their macromolecular constituents—such as proteins and nucleic acids. Macromolecules adopt defined three-dimensional architectures that dictate their functions and their mechanistic mode of action. Studying these 3D-structures at the atomic level allows gaining a deep insight into biological processes—such as how molecules interact with their ligands, how substrates are processed by enzymes, how molecules recognize and bind to other protein partners, how DNA is processed by the cell, and how macromolecular activity is regulated. Such molecular, mechanistic knowledge underpins most areas of modern biology. It also has applications in biotechnology and biomedicine, being critical for the rational design of therapeutic drugs, the (re)engineering of enzymes of industrial interest and, in some cases, to determine and understand the molecular cause of human disease.

Revealing the 3D-structure of a macromolecule implies that the coordinates (i.e. location in space) of each of its thousands of individual atoms must be determined. Visualizing a molecule at such atomic resolution requires a microscopic enlargement of approximately 10^7. This is not achievable by conventional microscopy and special methodologies are required. The most popular and successfully employed technique for this task is X-ray crystallography, which has yielded ca 90% of all protein structures elucidated to date. The technique undisputedly reaches the highest spatial resolution currently attainable, is economical and user-friendly. However, its application requires that the sample under study is first prepared in the form of a crystal, where multiple copies of the molecule are arranged in a highly regular lattice. The growth of such crystals is deterministic of the success or failure of the technique and, thus, the technique is not always applicable. Crystallographic structural analysis is closely accompanied by bioinformatic analysis of protein sequences and other sample data—jointly, these methods can produce an enriched view of the molecular world.

A fascinating discipline, X-ray crystallography brings together aspects of physics, chemistry, engineering, and computer programming in order to allow the study of the structure of biological matter. In this course you will gain a broad understanding of the theory and
practice of X-ray crystallography, as well as sample production, crystal growth and the bioinformatics analysis of the macromolecular structures produced.

2. Contents of the course:
The lectures and practical work held during the course cover the following topics:
Atomic structure of proteins; interpretation of a structural model; interactions of light (electrons, X-ray and neutrons) with proteins and its application to structural analysis; purification of proteins; crystallisation methods; diffraction of X-rays by crystals; the phase problem and its solution by heavy atom derivatives and Molecular Replacement; the calculation of electron density maps revealing the position of atoms in space; use of Linux for scientific work; modelling of a protein structure using computer graphics; refinement and validation of a 3D-structure; sequence analysis and alignment; dynamic programming; programming languages.

3. Previous knowledge
No previous knowledge is required. However, students wishing to engage in projects with a laboratory component would benefit from previous experience in general microbiological and biochemical preparation techniques: *E. coli* cultivation, chromatographic purification of proteins, electrophoresis.
It is recommended, but not required, to attend the lectures of Prof. K. Diederichs (“Bioinformatics” and “X-ray analysis of proteins”) as introduction to the topic of the course. In addition, attendance of “Mathematics for biologists“ is recommended. General mathematical knowledge of vectors, complex numbers, and simple statistics will be of advantage, but all required concepts will be revisited during the course.
Advanced Course "Molecular Genetics: Cell cycle regulation - from mechanisms to disease"

Coordinator: Prof. Dr. T.U. Mayer

Introduction:
The genetic integrity of each organism depends on the faithful segregation of its genome during mitosis and meiosis. Errors in this pathway can result in cancer formation or developmental defects. The aim of our research is to dissect the function and regulation of mitotic and meiotic proteins. Insights into mitotic and meiotic processes are not only important for a better understanding of the basic concepts of cell division, but also for the development of novel strategies for the treatment of cell cycle relevant diseases such as cancer.

Our research covers the following major lines of investigation:

1. Which are the key components required for the assembly of the mitotic spindle and how are they regulated?
2. What is the role of motor-proteins in chromosome congression and segregation?
3. How is the ubiquitin ligase APC regulated to ensure switch-like cell cycle transitions?

Course theory:
Eukaryotic cells – like any organism – face the challenge to make the right decisions, i.e. they have to adapt their cell cycle program to internal as well as external cues. Furthermore, once decisions are made they have to be irreversible to ensure that the different cell cycle events occur in the right order. Typical examples are the entry into M-phase or the metaphase-to-anaphase transition where cells have to wait until the last chromosome is correctly attached. Our interest is to understand the mechanisms underlying the decision process of mitotic as well as meiotic divisions, e.g. how do cells sense unattached chromosomes? How are the antagonistic activities of kinases and phosphatases regulated to ensure switch-like entry into M-phase? How do kinesins find the spindle equator? For these studies we combine classical cell-biology and molecular-biology approaches with state-of-the-art time-resolved 3D-microscopy techniques. In addition to classical approaches, the lab uses small molecules to modulate protein function in living cells. This approach, termed Chemical Biology, facilitates the modulation of protein function on a fast time scale. Compounds identified in our lab are not only of interest for basic research but also for the development of novel therapies in tumor treatment. During the course of the VTK, we invite 4 - 5 internationally renowned scientists from e.g. Stanford University, Yale University, Kings College London to present their work. This talks provide not only access to the latest scientific achievements and breakthroughs but also the opportunity to ask experts about their career and scientific history.

Literature:
"The Cell Cycle" by D. Morgan, Oxford University Press or our website: https://www.biologie.uni-konstanz.de/mayer/
Requirements:
Before the start of the VTK we will have a short meeting (please, check the black-board / your university email account for the announcement) where we will discuss the general outline of the course. Basic knowledge of cell biology, biochemistry, molecular genetics, and physiology (comparable to the content of respective courses in the Bachelor study courses “Biological Sciences” and “Life Science” at the University of Konstanz).

You will learn:

Scientific skills:
- Cell biological methods, e.g. tissue culture, transfections, stable cell line generation, cell engineering (CRISPR/Cas9), immunofluorescence
- Molecular biological methods, e.g. PCR, cloning, mutagenesis
- Biochemical methods, e.g. protein expression and purification in bacterial as well as in eukaryotic systems, in vitro enzyme assays
- Microscopy techniques, e.g. fluorescence time-resolved 3D imaging, high-resolution microscopy, quantitative image analysis,
- Chemical biology methods, e.g. compound handling, in vitro and in vivo small molecule inhibition studies, data handling, design and analyses of compound screens

Transferable Skills:
- You will learn how to prepare a poster and present your scientific data in our lab seminar
- You will have the chance to meet and talk to experts in the field of cancer drug development as well as young researchers working in the area of cell cycle research at internationally renowned research institutes
- You will learn how to present a manuscript in our journal club
- You will learn how to critically analyze and discuss scientific data
- You will be introduced to Excel, PowerPoint, and Adobe Illustrator to present your data in a professional manner
Advanced Course "Molecular Evolutionary Biology"

Coordinator: Prof. Dr. Axel Meyer

1. Topic of the course:
This course focuses on fundamental issues in evolutionary and developmental biology. The central aim of the course is to contribute to our understanding of the evolution of biodiversity. Specifically, the projects in the course will focus on the developmental, molecular, as well as genomic mechanisms of morphological and behavioral traits that differentiate species and other major groups of organisms. Students will have the unique opportunity to contribute to on-going studies of the molecular evolutionary biology underlying morphological adaptation and speciation. As part of the course, participants will take part in multidisciplinary research that integrates modern approaches in population genetics, molecular evolution, and molecular phylogenetics, comparative genomics and bioinformatics as well as includes work on the connections between developmental and evolutionary biology. The organisms that will provide the primary taxonomic focus of many projects include the zebrafish, live-bearing fish from the Neotropics, and the evolutionary highly successful cichlid fishes. Using these models, we will study how species form and how genomes change over evolutionary timescales. The course will be conducted in English, and it will have daily lectures on topics spanning the breadth of developmental and evolutionary biology. We will also conduct a weekly journal club in which we will discuss recent literature and students will also receive structured guidance on all steps from planning of experiments, to executing their study, to writing the final papers that detail their empirical findings. We hope to provide a stimulating and educational experience that highlights the excitement of doing organismal biology in the genomic age.

2. Techniques:
A large variety of questions and approaches will be utilized in the course. Student projects will exploit a diversity of techniques that are not only at the cutting edge of evolutionary and developmental biology but also increasingly essential in disciplines such as human genetics, toxicology, and personalized medicine. A large component of all projects will involve molecular techniques to determine and analyze population genetic data, characterize phenotypic and genomic variation among close relatives, and DNA sequence analysis. Instruction will also be provided for how to handle the large datasets (up to several million nucleotides) that often make up the core of biological research today. Several of the molecular biological techniques taught in this course will include the extraction of DNA, PCR-amplification of genes, and construction of c-DNA libraries. For gene expression analyses and developmental investigations, techniques such as whole mount in situ hybridization, quantitative PCR, microinjection into oocytes, and transcriptome assembly and analyses will all be taught. Computer-based investigations will include statistical evaluations of population genomic and phylogenomic data, and will also emphasize the analysis of genetic information retrieved from genomic databases for questions in comparative genomics and bioinformatics. Depending on the interests of the students, almost entirely "bench" or "computer" projects will be offered.
Relevant Literature:


**General literature:**


Advanced Course "Dynamics of aquatic ecosystems"

Coordinator: Prof. Dr. Frank Peeters

Research goals of the environmental physics group

Our research aims at a process based understanding of the dynamic interactions within aquatic ecosystems. Climate change, reduction in nutrient supply, and immigration of invasive species influence not only the abiotic conditions in the aquatic habitat but also the conditions for growth and the food web structure and thus alter the organismic interactions in lakes. To assess and predict the consequences of environmental change for lake ecosystems, we work on a mechanistic understanding of the role of nutrient and temperature distributions and of hydrodynamic conditions and mixing processes for the development and interactions of organisms within the ecosystem. In recent years a major research focus has also been on greenhouse gases in lakes and especially on the factors that influence the release of methane from lakes and reservoirs. Methane emissions from lakes and reservoirs are one of the most important natural sources of methane at a global scale.

Our research is strongly based on empirical data which are collected in field experiments. Thereby, we combine high-resolution measurements using probes equipped with in-situ measuring sensors that are deployed in moorings or operated from ships in a profiling mode, with laboratory analyses of water and zooplankton samples collected in the field. Lake research investigating ecosystem interactions under natural conditions differs from the research on laboratory systems, because it is usually impossible to control or deliberately influence the conditions affecting entire ecosystems. Therefore, we typically base our research on intensive empirical field investigations and combine data sets with numerical modelling to allow generalization of the results. In addition to field measurements we also conduct experiments in mesocosms to test hypothesis under controlled conditions.

Research questions in the course

Currently, we work on several topics that involve field experiments on Lake Constance and on small lakes in the Upper-Swabian Lake District, but we also work with mesocosms and with sediment cores in the lab. One research area is on plankton. We want to understand the influence of local sources of nutrients and water column properties on the spatial distribution and structure of the plankton community and the role of transport processes for the generation of heterogeneous plankton distributions, i.e. plankton patchiness. Another research topic concentrates on the question, why the toxic cyanobacteria P. rubescens, which is a dominant species in several pre-alpine lakes, does not establish large abundances in Lake Constance.

A second research area is on methane, particularly on the heterogeneous release of methane from sediments. The investigations are based on the collection of water samples that are analysed with gas chromatography, on installed instruments measuring methane and CO₂, and on ship based profiling with in-situ sensors. Recently, we started investigating the release of methane from sediment cores from different locations and under different conditions, which raised several question with respect to the consequences of climate warming.
and the impact of organisms in the sediments on methane release.

The third area of current research is the impact of surface waves on the littoral zone. Particular focus is on surface waves generated by ship traffic and the connection of these waves to erosion and drift of organisms in the shallow water zone. Wave properties and information on erosion can be derived from moored instruments in the shallow water zone. We also intend to test a new instrument for measuring wave motions off-shore and combine this with measurements on turbidity and erosion near shore.

Besides the observational research, another major focus of our research is numerical modelling addressing e.g. competition and predator-prey interactions in vertical water columns, the simulation of transport and ecosystem dynamics in three dimensions and surface waves and their impact. It is also possible to conduct projects in this area of research.

Work program

**Practical part:**

The students work in groups of two. They develop a work plan for their project, conduct the field and laboratory work and analyse the data with the support of a project supervisor. All projects are integrated part of our current research projects. After three weeks intermediate results are presented by the research groups and discussed with the other participants and supervisors of the course to adjust the remaining research program based on the information gained so far. At the end of the course the project results will be presented by the research groups in a poster session. Each group compiles and documents their data to make them available for further use in our research group. After the course the students provide a summary of their project work in the format of a scientific manuscript consisting of an abstract, an introduction providing the motivation of the project, a methods section, a section on the main results and a discussion.

**Theoretical part:**

**Lectures:**

Basic principles in physical limnology (exchange and transport processes, tracer techniques), relevance and release of methane, utilization of acoustic techniques in aquatic systems, plankton patchiness, waves and their ecological relevance, basic ocean dynamics, climate change, introduction to ecological modelling, case studies from specific lakes. The lectures not only present basic principles but will also show recent results from the current projects of the research group. We will have additional presentations from invited guests addressing specific research topics.

**Seminar:**

In the seminar the participants present selected articles relevant for their projects.

Additionally, the students will be introduced in a hands-on tutorial to the software MATLAB. This software is excellently suited for the analyses of large data sets and for numerical modelling and is not only used by our working group but also in many other research groups and in engineering.

**Aims of the course**

Development of an expertise to independently design and conduct limnological projects, that consider biotic and abiotic factors; experience with a wide variety of field techniques and the analysis of large data sets; familiarity with the interpretation of field data and the assessment of the relevance of abiotic conditions and physical processes for organismic interactions in lakes; understanding of the causes and consequences of dynamic interactions and of the implications of environmental change (climate warming, oligotrophication) on aquatic ecosystems.
Advanced Course "Cellular Biochemistry"

Coordinator: Prof. Dr. M. Scheffner

1. Introduction

Elucidation of the mechanisms controlling the activity of proteins and their interaction with other biomolecules in time and space has become a major focus of basic and applied research. The eventual function of proteins is regulated by various means, including protein folding and assembly into larger complexes, covalent modification (e.g. phosphorylation, covalent modification of proteins by ubiquitin and ubiquitin-like proteins), and modulation of protein stability.

The stability of intracellular proteins is mainly determined by the action of the ubiquitin-proteasome system. In this system, proteins are first modified by the covalent attachment of ubiquitin, an evolutionally conserved 76 amino acid polypeptide. This modification ("ubiquitination") then serves as a recognition signal for a multi-subunit protease complex, the 26S proteasome. Notably, ubiquitination of proteins frequently depends on their prior modification with other chemical entities. For example, several proteins involved in cell cycle regulation need to be phosphorylated in order to be recognized as substrate for ubiquitination and degradation. It has become increasingly clear that such combinations of posttranslational modifications play a decisive role in the control of many fundamental cellular processes thereby contributing to the functional plasticity of regulatory networks.

2. Content

a) Theoretical part: This part will be performed together w/ the Advanced Course "Cellular Biochemistry and Mass Spectrometry" (Prof. F. Stengel)

1. Enzymology and physiology of the modification of proteins by ubiquitin and ubiquitin-like proteins.

2. Methods used in the analysis of protein modification (e.g., mass spectrometry, unnatural amino acids).

3. Methods used in structural mass spectrometry (MS of intact assemblies, affinity purification and cross-linking coupled to MS, ion mobility MS).


5. Aspects of cancer biology including the role of human papillomaviruses and the ubiquitin-conjugation system.
b) Experimental part:
The actual topics of the student projects depend on ongoing research activities of the supervising doctoral researchers and postdoctoral fellows. Current research activities include:
1. Characterization of components of the ubiquitin system and their physiological function in vitro and in cell culture studies.
2. Role of the ubiquitin system in patho-physiological processes (cervical cancer, Angelman syndrome).
3. Unnatural amino acids as tools to study ubiquitination.

c) Methods:
- Biochemical and cell biological methods include:
  PCR, PCR-directed mutagenesis, cloning; expression of recombinant proteins in *E. coli*, insect cells (baculovirus system), or mammalian cells (transient and stable transfections; inducible expression systems); co-precipitation analyses, gel electrophoresis, Western-Blot, immunofluorescence; determination of the activity of enzymes of the ubiquitin system.
- Preparative and analytical methods include:
  Isolation and purification of proteins expressed in *E. coli*, insect cells, or mammalian cells by various chromatographic methods (e.g., ion exchange, size exclusion, affinity); mass spectrometry.
- Methods in proteomics and structural mass spectrometry:
  LC-MS/MS, label-free quantitation; computational analysis and data processing

3. Requirements
Basic knowledge of biochemistry (with an emphasis on protein structure and function), cell biology, molecular genetics, and physiology (comparable to the content of respective courses in the Bachelor study courses "Biological Sciences" and "Life Science" at the University of Konstanz).

4. Literature (preparatory)
L. Stryer, Biochemistry.
D. Voet & L. Voet, Biochemistry.
Advanced Course "Microbial Ecology and Limnic Microbiology"

Coordinators: Prof. Dr. David Schleheck and Dr. Nicolai Müller

1. Introduction

The majority of life on planet Earth is microbial, and the survival and growth of these organisms in complex communities and in diverse habitats require biochemical transformations. Hence, one central goal of the research done in our group is to discover and understand bacterial metabolism. For example, we investigate degradation pathways in anaerobic bacteria of the human gut for a transformation of dietary organosulfur compounds into harmful hydrogen sulfide, and pathways in aerobic and anaerobic environmental bacteria for a transformation of natural compounds or xenobiotic industrial chemicals, such as in Lake Constance. Other research done in the Schleheck group involves the phyto-, bacterio- and virioplankton community of Lake Constance and microbial biofilm formation and biofilm control. Therefore, our laboratory methods comprise bacterial cultivation and physiology, biochemistry, analytical chemistry, genomics and proteomics, but we analyse microbial communities also directly in their natural habitat. Ultimately, the accumulated knowledge should inform new approaches to improve human and environmental health as well as biotechnology.

Our present research covers the following areas:

- The **microbial biodegradation** projects cover organosulfonate (R-SO$_3^-$) substrates, such as taurine and sulfoquinovose, and organophosphonate (R-PO$_3^{2-}$) substrates, such as ciliatine. Further projects involve syntrophic fermentation in co-cultures and anaerobic utilization of acetone and of phosphite (projects led by Dr. Nicolai Müller). Here, as for one example shown in the Figure below, emphasis is put on a recently discovered process, that is ‘organosulfonate respiration’. This process is relevant in anoxic environmental habitats as well as in the human intestinal community and leads to the production of hydrogen sulfide: as opposed to using sulfate as electron acceptor for anaerobic respiration, these microbes make use of the organosulfonates as electron acceptor for their energy conservation. One pathway discovered in the human gut bacterium and opportunistic pathogen *Bilophila wadsworthia* employs a new, desulfonating glycyl-radical enzyme.
Figure 1. Metabolism of taurine and isethionate by the human gut bacterium *Bilophila wadsworthia*. (A) *B. wadsworthia* and other intestinal bacteria degrade dietary and host-derived organosulfonates in order to access sulfite as electron acceptor for their anaerobic respiration and produce harmful hydrogen sulfide (H\(_2\)S). (B) *B. wadsworthia* utilizes taurine and isethionate as electron acceptors through the glycyl radical enzyme (GRE) isethionate sulfite-lyase (IslA) with its GRE-activase component (IslB). The sulfite released by the GRE is reduced to sulfide by dissimilatory sulfite reductase (Dsr) and coupled to proton translocation for ATP synthesis (symbolized as [H\(^+\)]), when using electrons from oxidation of an alternative electron donor such as lactate (grey box). For comparison, the ATP-consuming activation of sulfate to sulfite is also shown. Other enzyme abbreviations: Tpa, taurine-pyruvate aminotransferase; Ald, alanine dehydrogenase; AdhE, CoA-acylating acetaldehyde dehydrogenase; Pta, phosphotransacetylase; AckA, acetate kinase; Sat, sulfate transferase; Apr, APS reductase.

- The diversity and seasonal succession of the zoo- and phytoplankton in Lake Constance is being well-studied since many years as part of a routine sampling program. However, the phylogenetic diversity and seasonal succession of the bacterioplankton community (size class 5 µm – 0.2 µm) in this lake has not yet been explored in such detail. We are establishing a much more detailed view on the recurrence and resilience of taxa within the annual plankton succession in Upper and Lower Lake Constance, by application of contemporary next-generation sequencing methods: the two lake basins differ in their morphology and physicochemical (nutritional) conditions, and we expect that the plankton succession in both basins differ due to differences in abiotic and biotic conditions. Furthermore, a much more fine-scaled correlation analyses is feasible regarding positive and negative interactions between phytoplankter, other protists and bacteria, reflecting competition,
grazing, and other interactions. The project is part of the RTG-R3 – *Resilience of Lake Ecosystems*. Most recently, we started to filter and collect also the virioplankton of Lake Constance (size class 200 nm – 10 nm).

- Biotic and abiotic surfaces in the environment are rapidly colonized by complex microbial communities. The process of **surface colonization and biofilm formation** provides numerous advantages to these organisms and supports critical ecological and biogeochemical functions. It also contributes to deleterious effects such as biofouling, biocorrosion, and the persistence and transmission of harmful or pathogenic microorganisms and of their genetic determinants. In the euphotic zone of aquatic habitats - such as in Lake Constance - these biofilm communities comprise photoautotrophic microorganisms, such as diatoms, green algae and cyanobacteria, which produce the organic carbon that fuels the life of a heterotrophic contingent of microorganisms, mostly bacteria. We study the initial colonization and formation of complex photoautotrophic-heterotrophic biofilm communities in our lake, as opposed to its planktonic microbial contingent (see above). We also examine designed, functionalized surfaces for their ability to prevent biofilm formation.

2. **Contents of the advanced course**

   a. **Theoretical part**
      

   b. **Experimental part**
      
      We study environmental bacteria, e.g. as isolated from water, soil, or the human gut, in our lab for their biodegradation capabilities and the underlying biochemical transformations, enzymes and genes. This includes growth of the strains in batch or continuous culture and quantifying biomass formation, substrate disappearance and product formation. In the past, bacterial pathways for degradation of industrial
chemicals and natural organo-sulfur compounds have been studied in aerobic as well as anaerobic strains, including the enzymes catalyzing these transformations. Our research involves also genome sequencing, proteomic and transcriptomic analysis, and production of enzymes by heterologous expression. Another research avenue aims at characterizing microbial communities directly in their environment (cultivation-independent), by total DNA extraction and meta-genomic sequencing (Bodensee plankton and biofilms).

Projects offered in the Advanced Course will be chosen based on the research currently being done in the lab. However, you are also strongly encouraged and highly welcome to propose your own research project; please discuss this with us in advance.

c. Methods

3. Required experience of participants
Participants should have taken at least one course in basic microbiology and should have experience in basic microbiological lab work (e.g., Microbiology-I lectures and the Kompaktkurs). Basic knowledge in chemistry and biochemistry is required for projects covering these areas. Experience in molecular biology and analytical chemistry is helpful.

4. Literature
Textbooks for general study:


For specific literature on our current research projects, please see our homepage, https://www.biologie.uni-konstanz.de/schleheck/publications/
Advanced Course in Chemical Ecology/Biological Chemistry

Coordinator: Prof. Dr. Dieter Spiteller

Introduction:

Chemical Ecology is an interdisciplinary research at the interface of biology and chemistry. It aims to reveal the chemical background of interactions between organisms. We identify compounds, such as antibiotics, toxins or signalling molecules. Next, we want to understand the biological function of identified metabolites.

Microorganisms, in particular Actinomyces, are well known as producers of both structurally highly diverse and pharmaceutically invaluable secondary metabolites. However, the role of such compounds for the producing organisms in their natural environment is largely unknown. Indeed, most natural products from microorganisms have been isolated from pure cultures. From whole genome sequencing projects, it was realised that most microorganisms have much more genes for secondary metabolite production than the number of compounds known from them. Microorganisms respond to abiotic factors or to other organisms - in symbiotic to pathogenic relationships - with induction of secondary metabolism and morphological changes. Thus, it is obvious that environmental factors trigger the production of secondary metabolites (Figure 1).

Our research about microbial chemical ecology contributes to the understanding of secondary metabolite formation, regulation and their function for the producing organisms.

Figure 1: Microbial Chemical Ecology – Organismic interactions

Current major research topics:

Chemical defence by microbial symbionts

In order to study the chemistry of microorganisms in symbiotic interactions we mainly investigate the symbiosis of leaf cutting ants with microorganisms. Leaf cutting ants grow a symbiotic fungus with leaf material. In turn the ants use their fungus garden as major food source. This mutualistic relationship is threatened by pathogens. However, leaf cutting ant associated microorganisms help to protect the fungus garden of the ants. We identified the first antifungal compounds from microbial symbionts in this interaction. Using bioassay-guided fractionation we found that many of the symbionts produce the well-known antifungal candididin macrolides (Figure 2).

However, the system is much more complex. There are many microorganisms involved and many pathogenic diseases. Thus, a multitude of antibiotic and antifungal compounds can be
expected from this ecosystem. Indeed, we already identified antimycins, valinomycins and actinomycins as additional antibiotics from leaf cutting ant symbionts (Figure 2). The specific fungal pathogen *Escovopsis weberi* produces secondary metabolites that support its attack of the garden fungus such as emodin, cycloarthropsone and shearinines. Besides the leaf cutting ants as the most studied model system, many more interactions in which microorganisms play a crucial role that have just not been studied so far can be expected. A systematic screening for symbionts among insects may reveal their microbial symbionts and their chemistry as well as novel antibiotics.

**Figure 2:** Antibiotics from microbial symbionts of leaf cutting ants: A) Biofilms on leaf cutting ants; B) LC-MS analysis and agar diffusion assay of an antifungal made by microbial symbionts; C) Antibiotics identified so far from *Streptomyces* symbionts of leaf cutting ants; D) Direct detection by MALDI (matrix assisted laser desorption ionisation) imaging

**Molecular basis of epiphytic microorganisms to protect their host plants against pathogens**
In this project we intend to reveal the molecular basis of the biocontrol function of selected epiphytic microorganisms that protect plants e.g. soy bean against pathogenic infections. For example, we recently identified the highly polar toxin 3-methylarginine using bioassay-guided fractionation in combination with HILIC HPLC (hydrophobic interaction liquid chromatography high performance liquid chromatography) (Figure 3). Since the chemistry of microbial epiphytes and endophytes is quite little studied, we expect that there is great potential to identify novel active substances from promising biocontrol organisms. Therefore, microorganisms associated with plants need to be isolated, characterised and tested for their biocontrol potential. Then extracts will be made and active compounds will be purified and identified. In order to understand the *in vivo* mode of action of biocontrol strains, knock-out mutants could be prepared and *in planta* experiments performed.
Figure 3: Epiphytes as biocontrol organisms: A) Bacterial blight of soy bean caused by the pathogen *Pseudomonas syringae* pv. *glycinea*, B) inhibition of *P. syringae* pv. *glycinea* by the epiphyte *Pseudomonas syringae* pv. *syringae* 22d/93, C) structure of the toxin 3-Methyl-L-arginine that inhibits the growth of *P. syringae* pv. *glycinea*, and D) 3-Methyl-L-arginine biosynthesis gene cluster

**Microbial reactions and adaptations to stress**

Abiotic factors such as heat, drought or heavy metal ions influence the growth of microorganisms and force them to adapt. We focused on *Streptomyces coelicolor* exposed to heavy metal ion stress. Stress by heavy metal ions can be studied under controlled conditions because heavy metal ions are just one defined factor that induces reactions in contrast to, for example, cocultivation where many possible factors may induce metabolic responses.

Testing a variety of heavy metal ions, Co$^{2+}$-ions turned out to cause the most pronounced effects leading to drastic metabolic changes that even led to new phenotypes. So far, we started metabolic profiling of the red phenotype. The red phenotype overproduces prodigiosins and in addition forms novel prodigiosin derivatives, coeligiosins.

Further experiments aim to fully characterise the induced secondary metabolites in response to heavy metal ion stress and to address their biological role.

**Induction of secondary metabolite production in coculture**

Microorganisms use intra- and interspecific chemical signals to coordinate their interactions with their environment. Using cocultivation assays we screen for metabolic or morphological changes that are induced when strains grow together (mimicking natural conditions).

Both bioassays and differential metabolic profiling by LC-MS are applied to identify the effects of cocultivation. Again we make use of bioassay-guided fractionation in order to isolate and characterise novel, induced secondary metabolites or the inducing signals.

**Degradation/Detoxification of natural products or xenobiotics by microorganisms**

We are also interested in how microorganisms degrade secondary metabolites and xenobiotics. For example, how anaerobic bacteria degrade sulfonates or if microbial symbionts contribute to detoxify xenobiotics.

**Methods:**
As interdisciplinary science at the interface between chemistry and biology Chemical Ecology requires an open minded, flexible approach to address research questions. In a problem-orientated way we combine techniques of organic chemistry, analytical chemistry, biochemistry, microbiology, molecular biology and ecology.

- Analytical chemistry (chromatography, HPLC, mass spectrometry, LC-MS, GC-MS, NMR)
- Organic synthesis (labelled compounds for biosynthetic studies, structure elucidation or material for biological testing)
- Microbiology (cultivation, isolation of microorganisms, PCR, cloning, mutagenesis, heterologous expression and functional characterisation of enzymes, genome mining)
- Ecology (biological function of natural products, bioassays)

Research Practical:
The course consists of a practical and theoretical part. You will work in close collaboration with a PhD student or Postdoc on a small research project of our current work that complements your supervisor’s work. Besides you will attend lectures/discussions, the group seminar and our literature seminar. At the end of your practical you will give an oral presentation and write a report of your experiments in the style of a paper. After the final submission of your report we will meet to discuss it.

The course aims to

- provoke further interest in the chemistry of biological systems
- provide experience in chemical ecology/chemical biology and interdisciplinary work
- provide hands-on experience in research work (experimental design, experimental practise, data analysis, critical interpretation of results, writing up results)
- make you familiar with new methods such as state of the art mass spectrometry
- prepare you for future independent research work (master, PhD thesis)

Your research project will be chosen as much as possible based on your interests, e.g. you may want to focus on analytical chemistry or you may decide to concentrate on molecular biology methods or a mixture of both.

Requirements:
In order to have a solid background for the course prior attendance of my lectures in Chemical Ecology and Chemistry and Biochemistry of Natural Products is required.

Solid knowledge and keen interest in organic chemistry, analytical chemistry, biochemistry, microbiology, and molecular biology is essential.

Literature:
At the beginning of the practical you will be provided with some key literature about your specific project and you will perform a literature search yourself.

P. M. Dewick, Medicinal natural products: a biosynthetic approach, 2009, 3rd edition, Wiley


1. Introduction

Protein complexes are at the center of all biological processes within a cell. Deciphering their composition, architecture, and assembly is key to understand their function. Here, emerging methods in mass spectrometry pose an exciting alternative due to their low sample requirements and comparatively high measuring speed.

In this course, the students will get to know and use classical biochemical techniques in combination with novel mass spectrometric and proteomic approaches in order to quantitatively study the content, interactions and dynamics of protein complexes involved in proteostasis and signaling. The students will also participate in another main focus of the group, which is the development and application of tailored chemical molecules to gain insights into the mechanistic principles of large and biologically relevant protein assemblies in health and disease.

2. Content

a) Theoretical part: This part will be performed together w/ the Advanced Course "Cellular Biochemistry" (Prof. M. Scheffner)

1. Enzymology and physiology of the modification of proteins by ubiquitin and ubiquitin-like proteins.
2. Methods used in the analysis of protein modification (e.g., mass spectrometry, unnatural amino acids).
3. Methods used in proteomics and structural mass spectrometry (principles of mass spectrometry, basic proteomic workflows, methods in structural mass spectrometry).
5. Aspects of cancer biology including the role of human papillomaviruses and the ubiquitin-conjugation system.

b) Experimental part:

The actual topics of the student projects depend on ongoing research activities of the supervising doctoral researchers and postdoctoral fellows. Current research activities include:

1. Architecture and structural dynamics of core components of the translational and signal transduction machinery
2. Studying the dynamics of intact protein complexes by quantitative cross-linking mass
spectrometry.

3. Application and development of novel cross-linkers for the analysis of proteasomal assemblies.

4. Unnatural amino acids as a tool to study the influence of specific PTMs.

c) Methods:
- Methods in proteomics and structural mass spectrometry:
  Cross-linking coupled to MS, shotgun LC-MS/MS, label-free quantitation; computational analysis and data processing;
- Click Chemistry
- Bioinformatics: cross-linking guided integrative modeling.
- Biochemical and cell biological methods include:
  PCR, cloning; expression of recombinant proteins in E. coli and S. cerevisiae; co-precipitation analyses, gel electrophoresis, Western-Blot, immunofluorescence.
- Preparative and analytical methods include:
  Isolation and purification of proteins expressed in E. coli or S. cerevisiae by various chromatographic methods (e.g., ion exchange, size exclusion, affinity); mass spectrometry.

3. Requirements
  Basic knowledge of biochemistry (with an emphasis on protein structure and function), cell biology, molecular genetics, and physiology (comparable to the content of respective courses in the Bachelor study courses "Biological Sciences" and "Life Science" at the University of Konstanz).

4. Literature (preparatory)
  E. de Hoffman & V. Stroobant, Mass Spectrometry.
  L. Stryer, Biochemistry.
  D. Voet & L. Voet, Biochemistry.
Advanced Course “The role of microbes in stress response and resilience of aquatic metaorganisms”

Coordinators: Prof. Dr. Christian R Voolstra
Dr. Anny Cardenas
Dr. Claudia Pogoreutz
Dr. Nils Rädecker

1. Introduction
Recent years have brought a changing imperative in life sciences sparked by the revolution of genomic tools to study the molecular setup of organisms. The development of next-generation sequencing changed our understanding of microbial diversity associated with organisms and environments. There is now a multitude of studies that support the notion that host-specific microbial consortia (‘microbiomes’) are associated with all multicellular organisms and provide functions related to metabolism, immunity, and environmental adaptation. Consequently, the biology of animals and plants must be understood in light of the host and its associated microbial consortia, the so-called ‘metaorganism’. The research interest of our group builds around this new concept. Our focus is to understand the structure and function of microbial associates and how they support host physiology and adaptation to changing environments. In particular, we study coral metaorganisms (composed of the coral animal host, intracellular photosynthetic dinoflagellate algae, and associated bacteria), which form the keystone species of reef ecosystems. Broadly, our lab follows three research areas: Research area 1 focuses on the development of novel methods to delineate the function and identity of aquatic metaorganism member species. Research area 2 is centered around the employment of model system-assisted approaches (manipulate gene function, microbial association, nutrient exchange) using seawater and freshwater anemones (Aiptasia and Hydra) to understand building principles and regulatory mechanisms of phototroph-heterotroph symbioses. Research area 3 is focused on the development of frameworks and diagnostics that support climate change resilience using field-based physiological and genomic coral reef surveys.

2. Contents
Students will have the unique opportunity to participate and contribute to on-going research projects. The course will be in English and it will consist of daily lectures on topics related to metaorganism structure/function/adaptation, coral reef ecosystems, climate change, symbiosis, genomics, mining ‘big data’, bioinformatics, and statistics. We will conduct a ‘journal club’ where participants present research papers to discuss current literature, and students will present their results in a ‘lab seminar’ designed to learn to critically examine the research conducted and the results obtained. Based on their research projects, participants are expected to write a concise research paper (Introduction, Material & Methods, Results, Discussion) that detail their empirical findings. For all aspects, students will receive structured guidance and supervision.

3. Expected background knowledge / Requirements
- Basic knowledge in molecular biology/genetics is expected.
- To pass the course, the following requirements need to be met:
  - Active participation in the lectures
- Power point presentation in the journal club and lab seminar
- Actively conducting research and presentation of the project results in the form of a (concise) scientific paper

4. Literature


Ziegler M, Seneca FO, Yum LK, Palumbi SR, and Voolstra CR. 2017. Bacterial community dynamics are linked to patterns of coral heat tolerance. *Nature Communications* 8:14213. 10.1038/ncomms14213


Advanced Course "Organismal Biology: Going wild" 2020

Coordinator: Dr. Lucy Aplin

Supervisors: Dr. Dina Dechmann, Prof. Martin Wikelski (Lehrstuhl Ornithologie, University of Konstanz and Max Planck Institute of Animal Behavior)

Introduction:

Only by studying animals in situ can we fully understand their behaviour in the context of life history and ecology. Yet field studies, whether observational or experimental, come with unique challenges at all stages - in study design, during data collection and with analyses.

In the upcoming “going wild” Vertiefungskurs we will take you to the field to work with wild animals and introduce you to the life of a field biologist studying animals in their natural habitat. This includes all the steps a scientist goes through from data collection to analysis. We will invest some time in the beginning observing the natural foraging and breeding behaviour of local birds. During a study design phase, we will review current literature and conduct round-table discussions in a problem-based-learning approach. You will go ‘into the field’ to collect data on the behavioural ecology of wild birds, with an aim to understanding how they respond to environmental variation and what role of behavioural plasticity and learning might have in shaping this response. In the second half of the course, we will analyze the data we have collected, working together as group to learn about, select and implement effective analytical techniques. Finally, you will present your findings together in a talk at the Max Planck Institute for Animal Behaviour.

In this course you will have the opportunity to observe and conduct an experimental and/or observational study on tits (paridae: Cyanistes caeruleus and Parus major) in the forest surrounding the Max Planck Institute in Moggingen. We have been monitoring a study population of great tits (Parus major) in the forest at Moggingen over several years. We use bird-rings and micro-chip tags to track individuals throughout their lifetime, and use a combination of observational data and experiments to study questions about sociality, information use and cognition. Paridae are a model system in evolutionary and behavioural ecology, and our study population is one of many across Europe. This course will introduce you to the long history of research on this model species, and you will learn about the very important contribution work on this species has made to our understanding of plasticity, selection and adaptation in the modern world.

You will come away from this with not only with a great experience but also a hands-on one. A first crucial part of this is to teach you critical thinking when setting up a study - targeted methods are needed to give you the best data in order to answer the question you want to answer and a considered design will give you enough power to run a proper analysis. Second, things inevitably don’t go completely to plan with fieldwork – it rains, animals don’t behave as you expect and a multitude of unexpected factors affect your results. This course will teach you problem-solving skills, lateral thinking and resilience in data collection. Lastly, once you have our data, you will work together to identify and work through the analytical challenges and opportunities arising out of exciting, but potentially ‘messy’, wild data, before presenting your findings to a scientific audience.