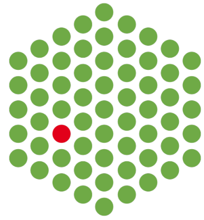
Abstracts presented at the

18th EMBL PhD Symposium

Life by Numbers
Towards Quantitative Biology

EMBL Heidelberg, Germany
17–19 November 2016

Organised by:
EMBL PhD Class of 2015

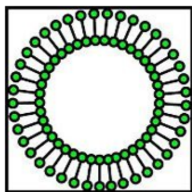
EMBL 

Also kindly supported by

Gold sponsors

The Company of Biologists

Silver sponsors



Avanti®
POLAR LIPIDS, INC.

Galton Institute

Bronze sponsors

BIO TREND

Prizes kindly offered by

Also kindly supported by:

EMBL CPP's founder parters

EMBL CPP's corporate partners

BD

Boehringer Ingelheim

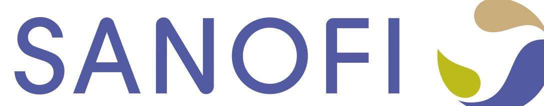
illumina®

ThermoFisher SCIENTIFIC

EMBL CPP's associate partners

eppendorf

MERCK



Contents

Symposium Organisers **6**

Welcome **7**

Acknowledgements **9**

Programme **10**

Day 1: Multilevel System Regulation **15**

Day 1: Data Management and Interpretation **27**

Day 2: From Genome to Proteome **37**

Day 3: Cell Communication Shaping Tissues **57**

Posters **76**

General Information **140**
Health and Safety Notes 141
Getting to EMBL 142
Poster Session Information 146
Information for Speakers 147
Questionnaires & Badges 148
Useful Telephone Numbers 149
Tourist Information 150

Participants **152**

Symposium Organisers

Ashna Alladin
EMBL Heidelberg, Germany

Renato Alves
EMBL Heidelberg, Germany

Chiara Baccin
EMBL Heidelberg, Germany

Theocharis Efthymiopoulos
EMBL Heidelberg, Germany

Buesra Erarslan
EMBL Heidelberg, Germany

Elisa Gallo
EMBL Heidelberg, Germany

Sebastian Henkel
EMBL Heidelberg, Germany

Christine Ho
EMBL Heidelberg, Germany

Bernhard Hoermann
EMBL Heidelberg, Germany

Eleni Kafkia
EMBL Heidelberg, Germany

Sandra Kozak
EMBL Hamburg, Germany

Piotr Krzywkowski
EMBL Monterotondo, Italy

Jakub Macosek
EMBL Heidelberg, Germany

Karen Katrina Manalastas
EMBL Hamburg, Germany

Daniel Elias Martin Herranz
EMBL-EBI Cambridge, United Kingdom

Sofya Mikhaleva
EMBL Heidelberg, Germany

Enric Mila Vilalta
EMBL Heidelberg, Germany

Chiara Morelli
EMBL Monterotondo, Italy

Øyvind Ødegård
EMBL Heidelberg, Germany

Julia Peukes
EMBL Heidelberg, Germany

Luca Rappez
EMBL Heidelberg, Germany

Allyson Ryan
EMBL Heidelberg, Germany

Sanjana Singh
EMBL Heidelberg, Germany

Anna Sueki
EMBL Heidelberg, Germany

Jervis Thevathasan
EMBL Heidelberg, Germany

Lara Urban
EMBL-EBI Cambridge, United Kingdom

Britta Velten
EMBL Heidelberg, Germany

Carina Vibe
EMBL Heidelberg, Germany

Ambra Villani
EMBL Heidelberg, Germany

Ranjith Viswanathan
EMBL Heidelberg, Germany

Nadezda Volkova
EMBL-EBI Cambridge, United Kingdom

Welcome

Welcome to the 18th International EMBL PhD Symposium that builds on the experience and tradition of a professional conference series initiated by EMBL Predocs for PhD students from all over the world. Since its inception in 2000 this conference series has grown into a well-known feature of the EMBL International PhD Programme. As a matter of honor and pride each class of first year Predocs strives to surpass the successes of previous classes.

In recent meetings we were taken on a journey “From Science Fiction to Science Fact”, learned about the “Rhythm of Life”, were invited to “Overcome Chaos”, talked about “Competition in Biology”, got “Inspired by Biology” while exploring nature’s toolbox, reflected on the extent to which “Chance” shapes biology and finally will delve into quantitative biology by looking into “Life by Numb3r5”.

The quantitative focus chosen for this year’s symposium reflects on the ever growing possibilities to target system-wide approaches towards understanding and modeling living processes. This is ultimately enabled by producing and integrating big data towards permitting theoretical predictions for the functioning of pathways, organelles, cells and even organisms. Consequently, the symposium builds on four major modules starting with “Multilevel System Regulation” followed by a session on “Data Management and Interpretation” before diving deeply into biology and taking us up on a journey “From Genome to Proteome” that will be concluded by an exploration on “Cell Communication Shaping Tissues”.

As with previous years I am impressed by and grateful for the amazing list of speakers who accepted the invitation from EMBL’s Predocs dedicated to turn this conference into a memorable experience for all of its participants. Please join me in using every opportunity throughout these three symposium days to enjoy the vibrant atmosphere of this extraordinary event. There will be a well balanced mix of different meeting formats, plenty of opportunities to learn about and discuss scientific progress and to enjoy the breadth of activities perfecting the event ranging from science slam to symposium party and beyond.

Wishing you a successful and inspiring meeting

Helke Hillebrand
Academic Coordinator and Dean of Graduate Studies at EMBL
October 2016

EMBL Predoc class of 2015

Acknowledgements

We would like to acknowledge everyone who came together to make the 18th EMBL PhD Symposium "Life by Numbers - Towards Quantitative Biology" possible.

First of all, thank you to the members of the 17th EMBL PhD Symposium Organising Comittee whose advice was essential to the smooth planning and progression of the symposium.

Thank you to EMBL's corporate sponsors, who made significant contributions to our symposium: Olympus, Leica, BD, Boehringer Ingelheim, GSK, illumina, ThermoFisher, Eppendorf, Merck, Nikon and Sanofi. We would also like to thank our external sponsors, the Company of Biologists, AHF, Avanti Polar Lipids and Biotrend for their generous financial support. We are also grateful to GeekWrapped for donating prizes.

We are honoured by the many exciting speakers who accepted our invitation to share their research with us. Special thanks to EMBO for supporting the EMBO Keynote Lecture and the EMBO Young Investigator Lecture.

Additionally, the support of the EMBL Finance Office, Grant Services, Photolab, Catering team and Reception staff has been invaluable. Shout out to Raffaele Totaro! A big thank you to Christina Dolt and all of the EMBL Course and Conference members for sharing their experience with us.

We also want to specifically acknowledge Balint Balazs and Sascha Meiers for their contributions to the website and abstract book.

We would like to thank EMBL, particularly the EMBL International PhD program, for giving us the opportunity to organise this symposium. We are especially grateful for the support from the Dean of Graduate Students Helke Hillebrand, as well as Meriam Bezohra and Matija Grgurinovic from the Graduate Office. We also greatly appreciate the understanding and patience shown by our supervisors during the organisation of this symposium.

Finally, we would like to acknowledge all of our participants. Thank you for being here, especially those who have contributed to the poster session and short talks. We hope you will enjoy the symposium!

18th EMBL PhD Symposium Organising Committee

Programme

Thursday, 17th November 2016

08:00-09:00	Registration
09:00-09:30	Symposium Opening & Welcome

Multilevel System Regulation

09:30-10:30	**T1 Keynote Lecture:** Lakshminarayanan Mahadevan *On the growth and form of the gut*
10:30-10:45	**T2 Short Talk:** Svend Dahl-Jensen *Deconstructing the formation of the ductal network in the pancreas*
10:45-11:15	Coffee Break
11:15-12:00	**T3 Lecture:** Lucas Pelkmans *Emergence of predictable patterns of cell-to-cell variability amongst genetically identical mammalian cells*
12:00-12:15	**T4 Short Talk:** Christoph Fritzsch *Modulation of transcriptional bursting by estradiol at a single endogenous allele*
12:15-13:45	Lunch
13:45-14:30	**T5 Science and Society:** Jonas Hartmann *Philosophy for Science: Can scientists rediscover the philosophy of science for themselves?*

Data Management and Interpretation

14:30-15:15	**T6 Lecture:** Jean-Karim Hériché *Systems biology of mitosis: a data perspective*
15:15-15:45	Flash talks

15:45-16:45	Poster Session 1 (Coffee Break)
16:45-17:30	**T7 Lecture:** Peter de Peinder *Life is great but complex... like quantitative vibrational spectroscopy*
17:30-17:45	**T8 Short Talk:** Klaus Yserentant *Towards quantitative 3D fluorescence microscopy with CoPS and array tomography*
17:45-18:00	**T9 Short Talk:** Sarah Noel Galleguillos *Quantifying cellular robustness in genome-scale metabolic reconstructions*
18:00-18:15	Thank the speakers
18:15-19:00	Blackboard Session
19:00-20:00	Dinner
21:00	Science Show

Friday, 18th November 2016

From Genome to Proteome

09:00-10:00	**T10 EMBO Keynote Lecture:** Luis Serrano *Transcriptome analysis of a small bacterium reveals non-TF predominant regulation which could be an ancient mode of responding to medium perturbations*
10:00-10:45	**T11 Lecture:** Leïla Perié *Deciphering the hematopoietic differentiation pathway at the single cell level*
10:45-11:15	Coffee Break
11:15-12:00	**T12 Lecture:** Leonie Ringrose *"In vivo biochemistry": Absolute quantification and kinetic modelling applied to Polycomb and Trithorax regulation*
12:00-12:15	**T13 Short Talk:** Lara Urban *Prediction of rare regulatory variants using deep learning*
12:15-13:45	Lunch

13:45-14:30	**T14 Science and Society:** John Liebler *OK, but what does it look like?*
14:30-14:45	**T15 Short Talk:** Tadek Krassowski *Breaking the genetic code: Multiple reassignments of the codon CUG during yeast evolution*
14:45-15:15	Flash talks
15:15-16:15	Poster Session 2 (Coffee Break)
16:15-17:00	**T16 EMBO Young Investigator Lecture:** Paola Picotti *Monitoring protein structural changes on a large scale*
17:00-17:15	**T17 Short Talk:** Andrew Tuckwell *An engineering approach to molecular assembly of the type 3 secretion system*
17:15-17:30	**T18 Short Talk:** Éric Durandau *Dynamic measurement of kinase activity in live single cell*
17:30-18:15	Blackboard Session
18:15-18:45	Panel Discussion (TTS)
18:45-19:00	Thank the speakers
19:00-20:00	Dinner

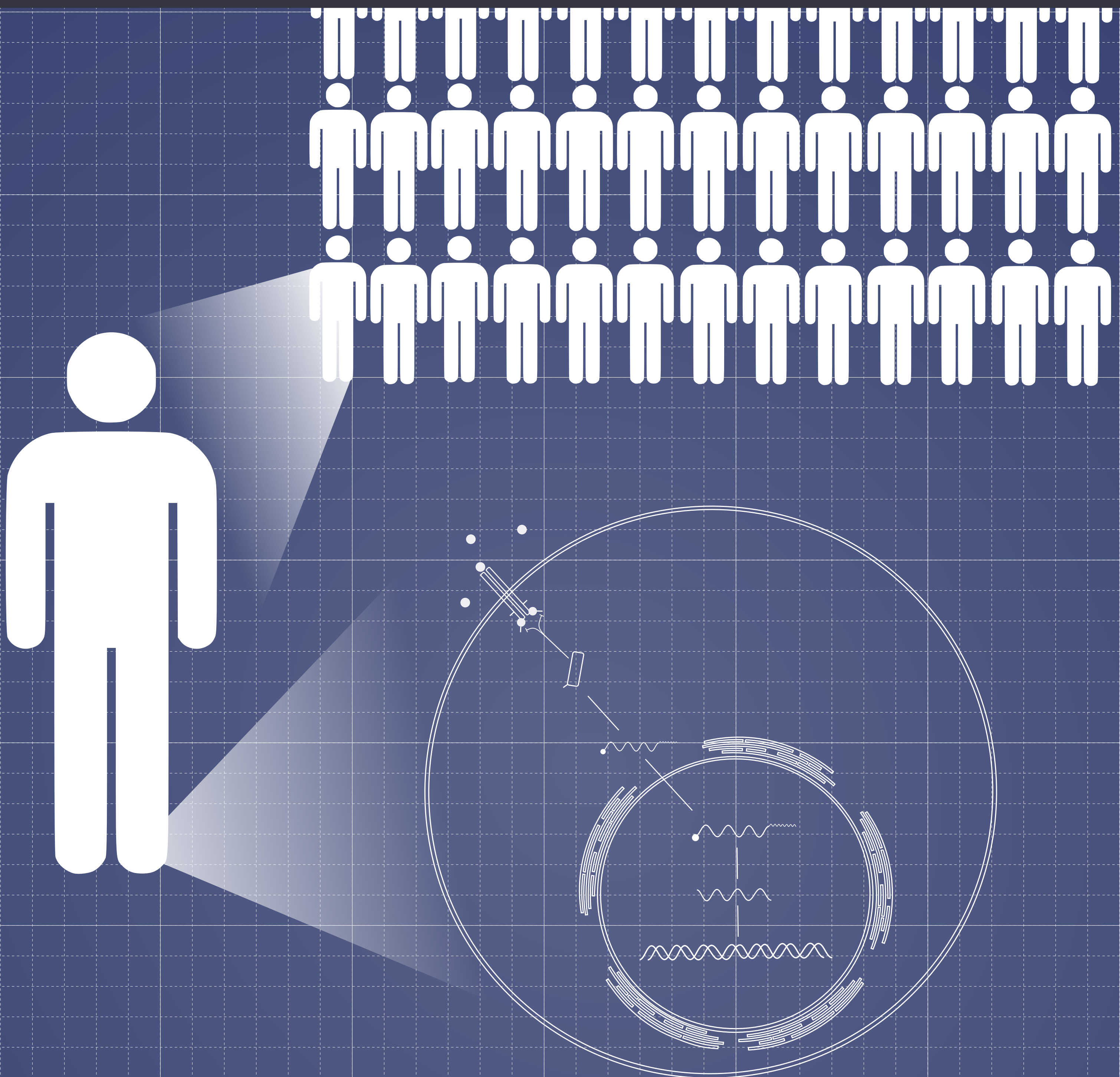
Saturday, 19th November 2016

Cell Communication Shaping Tissues

09:00-10:00	**T19 Keynote Lecture:** Raymond E. Goldstein *Upside Down and Inside Out: The biomechanics of cell sheet folding*
10:00-10:45	**T20 Lecture:** Dagmar Iber *From Networks to Function – Computational models of organogenesis*
10:45-11:15	Coffee Break
11:15-12:00	**T21 Lecture:** Irene Miguel-Aliaga *Homeostatic plasticity*

12:00-12:15	**T22 Short Talk:** Erika Tsingos *How tissues coordinate growth in an organ: Insights from modeling clonal lineages in fish*
12:15-13:45	Lunch
13:45-14:30	**T23 Science and Society:** Russ Hodge *How to see a ghost, think like a molecule, and write like a scientist*
14:30-14:45	**T24 Short Talk:** Gabriel Cavalheiro *Myc transcription factors regulate mouse lens development and eye organogenesis*
14:45-15:15	Coffee Break
15:15-16:00	**T25 Lecture:** Timothy A. Ryan *Power supplies for brain cells: the cost of thinking*
16:00-16:15	**T26 Short Talk:** Jason Cosgrove *Mapping the distribution of chemokines in lymphoid tissues: Combining super-resolution imaging with multiscale modelling*
16:15-16:30	**T27 Short Talk:** Amit Singh *Growth and form in 4th Dimension: Non-invasive, in vivo quantification of growth anatomy and morphology through time*
16:30-17:00	Coffee Break
17:00-17:45	Blackboard Session
17:45-18:15	Panel Discussion (TTS)
18:15-18:30	Thank the speakers
18:30-19:00	Award Ceremony
19:00-20:00	Dinner
21:00	Closing Party

Day 1 (morning): Multilevel System Regulation



Lakshminarayanan Mahadevan

Harvard University
Cambridge, MA, United States of America

Professor Mahadevan graduated from the Indian Institute of Technology, Madras, and then received an M.S from the University of Texas at Austin, and an M.S. and Ph.D. from Stanford University in 1995. He started his independent career on the faculty at the Massachusetts Institute of Technology (MIT) in 1996. Professor Lakshminarayanan Mahadevan is currently the Lola England de Valpine Professor of Applied Mathematics, Organismic and Evolutionary Biology and Physics at Harvard University. His work centers on using mathematics to understand the organization of matter in space and time.

T1 Keynote Lecture

On the growth and form of the gut

Mahadevan, Lakshminarayanan

Harvard University , United States of America

November 17th, 09:30

During development, the vertebrate gut starts out as a simple tube that lengthens, coils and gets patterned internally with absorptive villi. I will first discuss how a minimal physical picture based on differential growth systematically breaks various spatial symmetries and allows us to quantify this process. This yields testable experimental predictions borne out in an organism (the chick) over developmental time, and across species such as birds, reptiles, amphibians and mammals. I will then show how shape feeds back on tissue fate in the context of stem cell niches that eventually populate intestinal crypts. Finally, I will discuss a molecular basis for the control of loop size and shape, and show how manipulating specific morphogenetic signals allows us to change intestinal morphology, suggesting a possible evolutionary pathway for morphological diversity.

T2 [P16] Short Talk

Deconstructing the formation of the ductal network in the pancreas

Dahl-Jensen, Svend; Sever, Dror; Flasse, Lydie Carole; Larsen, Hjalte List; Grapin-Botton, Anne; Sneppen, Kim

Center for Stem Cell Decision Making (StemPhys), Denmark

November 17th, 10:30

Branched structures are ubiquitous in biology and include the lung, exocrine glands and various ductal systems. They serve as conduits for fluid transport and play a critical role in physiological processes. The dominant theoretical framework for ramification posits a reaction-diffusion mechanism driven by diffusion limited aggregation. However, recent evidence suggests that mechanical effects are important in the process. We have developed a method for mapping the tubular network of the pancreas from three-dimensional images at different stages in the developing organ. The tubular network of the pancreas is digitized by mapping the intersections and terminal end of the pancreas as Lumen Nodes (LNs) and connecting them though ducts. The resulting networks have some striking properties with two main conclusions: 1. Even though the shape of the pancreas differs between individuals, the networks at the same stage share stereotypic traits 2. These traits change during development. To support this finding we have developed an *in silico* model that recapitulates the development of the tubular network. While the pancreas is growing, the LNs, represented as subcellular elements, increase in number and connect with each other and interact following a Morse-like potential. When the plexus is formed it is then pruned to become a tree-like network. The results show that the model can successfully recapitulate key elements of the developing pancreatic tubular network. The model predicts that redundant duct connection followed by flux based pruning can accurately describe pancreas tubulogenesis. Our results are compatible with a pruning that would be driven by fluid secretion from acinar cells at the tips of the ducts.

Lucas Pelkmans

Institute of Molecular Life Sciences, University of Zürich
Zürich, Switzerland

Professor Pelkmans studied at the University of Utrecht in The Netherlands and obtained his PhD from the ETH Zurich in 2003, after which he got a position as a postdoctoral fellow at the Max Planck Institute of Molecular Cell Biology and Genetics in Dresden, Germany. In 2005 he became assistant professor at the ETH Zurich and in 2010 the full professor at the University of Zurich, where he currently holds the Ernst Hadorn Chair. His lab operates at the forefront of research in quantitative cell biology, in the study of cell-to-cell variability, as well as in systems approaches based on large-scale genetic perturbations and network biology.

T3 Invited Speaker

Emergence of predictable patterns of cell-to-cell variability amongst genetically identical mammalian cells

Pelkmans, Lucas

Institute of Molecular Life Sciences, University of Zürich, Switzerland

November 17th, 11:15

My lab has had a long-standing interest in how, within a population of genetically identical mammalian cells grown under identical conditions, predictable patterns of cell-to-cell variability can repeatedly emerge. In contrast to assuming a largely stochastic and thus unpredictable behavior at the single-cell level, we focus on identifying deterministic sources of cell-to-cell variability that stem from the cellular state and the population context. More recently, we have expanded on this work by uncovering a system by which single cells couple the sensing of local cell crowding to gene expression and a subsequent adaptation of membrane lipid composition, which feeds back on the sensing mechanism itself. Through computer simulations and experimental confirmation, we find that this cell-autonomous system can drive the emergence of gradual patterns of gene expression and signaling in a population of genetically identical cells. Furthermore, I will use the system that we uncovered to highlight the importance of time-scale adaptation in signal processing, and put forward to concept that the plasma membrane acts as a tunable capacitor to accomplish this.

T4 Short Talk

Modulation of transcriptional bursting by estradiol at a single endogenous allele

Fritzsch, Christoph; Baumgärtner, Stephan; Legewie, Stefan; Reid, George

Institute of Molecular Biology Mainz, Germany

November 17th, 12:00

Dynamic observations of transcription across multiple species revealed that transcription is often discontinuous and occurs in short bursts that are interspersed by long episodes of gene inactivity. It is assumed that the stochastic timing of these events leads to heterogeneous gene expression patterns within cell populations and across time. However, it is less clear how cells modulate transcriptional bursts to accommodate gene expression changes in response to signals in such a stochastic regime. We created a reporter cell line to monitor estrogen dependent transcriptional bursts in individual living cells. The knock-in of PP7 sequences into a single allele of an Estrogen Receptor alpha target gene and co-expression of fluorescently labeled PP7 coat proteins in MCF-7 breast cancer cells enables imaging of nascent transcripts and thereby, stochastic gene activity, over time. Different stimuli conditions were tested to probe the effect of estrogen on transcriptional bursting. The resulting data was used to inform a stochastic model of promoter progression and transcription. Both burst size and burst frequency are regulated in response to increasing estrogen concentrations. In addition to the gene intrinsic stochasticity, cell to cell variability in the kinetic parameters was needed to fully explain experimental observations. This finding was also confirmed in an independent cell line with two labeled alleles. It is therefore suggested, that kinetic parameters of bursts are not only modulated in response to signals, but that they are themselves subject to cell-to-cell variability. Such information on allele extrinsic variability in gene dynamics is only possible through the use of time resolved analysis in multiple single cells. Therefore, this study highlights the important role that dynamic measurements play in today's single cell biology.

Jonas Hartmann

EMBL Heidelberg
Heidelberg, Germany

Following his apprenticeship as a restaurant chef, Jonas Hartmann decided to study cell biology, receiving his master's degree from the University of Zurich in 2014. As a PhD student at EMBL, he is now investigating the interplay of signaling and morphogenesis, developing experimental and computational tools for single-cell perturbation and analysis. However, his fascination with philosophy also has Jonas ask some very different questions, including how the paradigms of modern biology were established, how they shape today's research, and how their limitations might be overcome. He is convinced that an understanding of such questions can help us do good science.

T5 Invited Speaker

Philosophy for science: Can scientists rediscover the philosophy of science for themselves?

Hartmann, Jonas

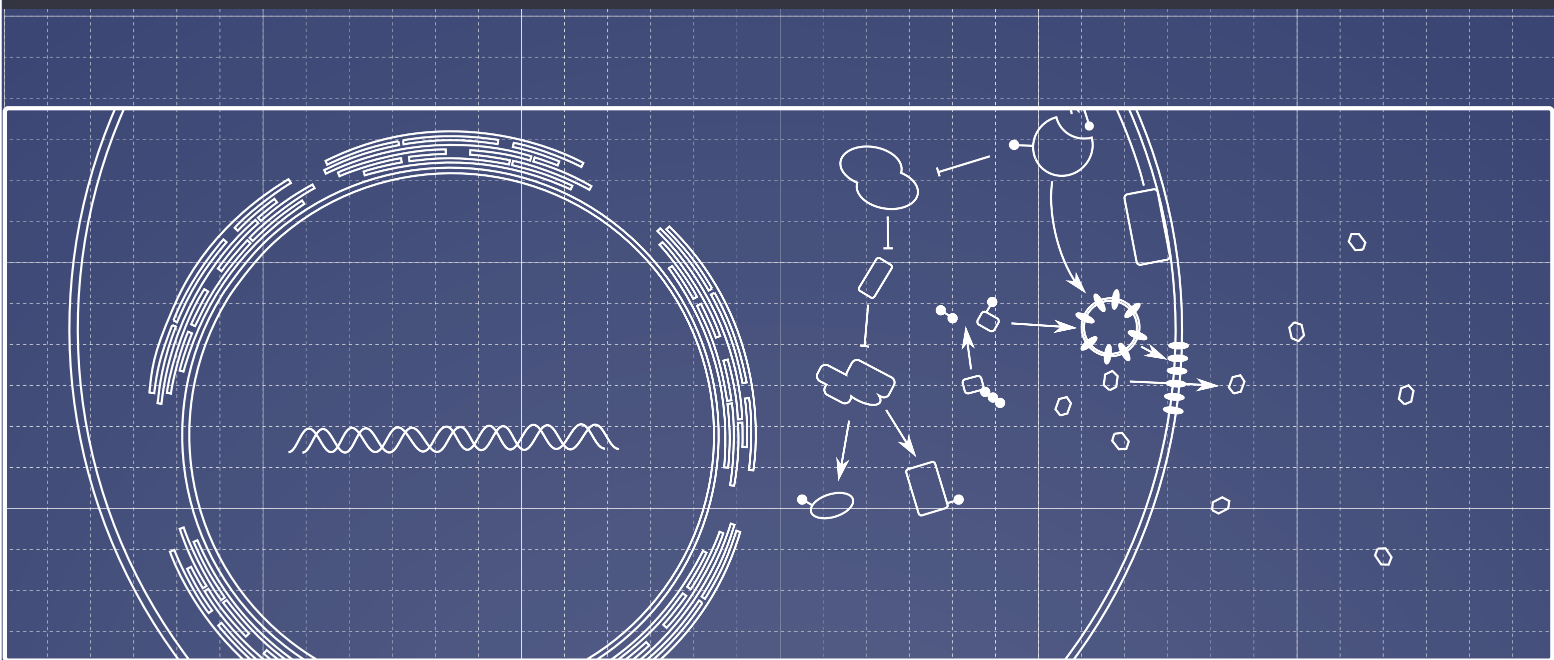
EMBL Heidelberg, Germany

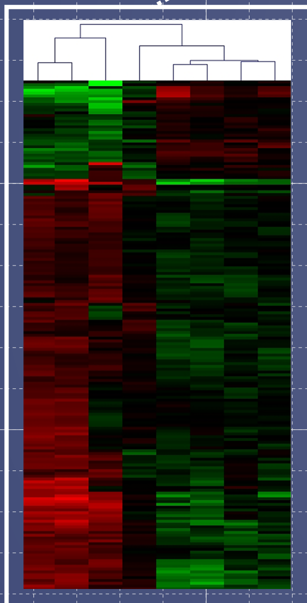
November 17th, 13:45

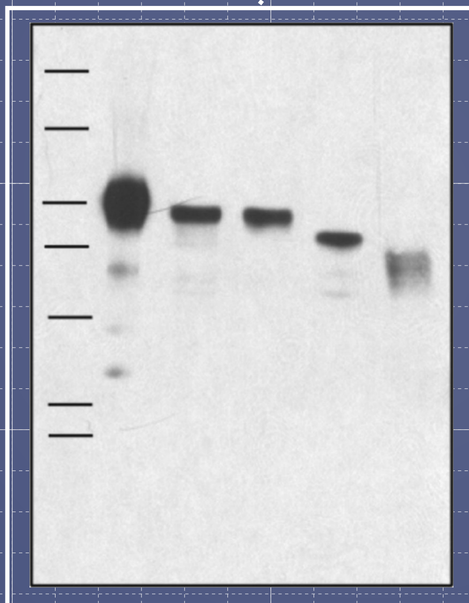
The rapid growth and diversification of the natural sciences in the past century brought with it an ever-expanding divide between science and philosophy. Today, this divide is apparent in both the teaching and practice of science: university curricula at best touch upon philosophy in tangent, and scientists rarely employ philosophical methods or ask philosophical questions with respect to their work. Conversely, philosophers of science are often content to study recent trends or ethical and societal impacts, but rarely have the aspiration of themselves contributing to the advancement of science.

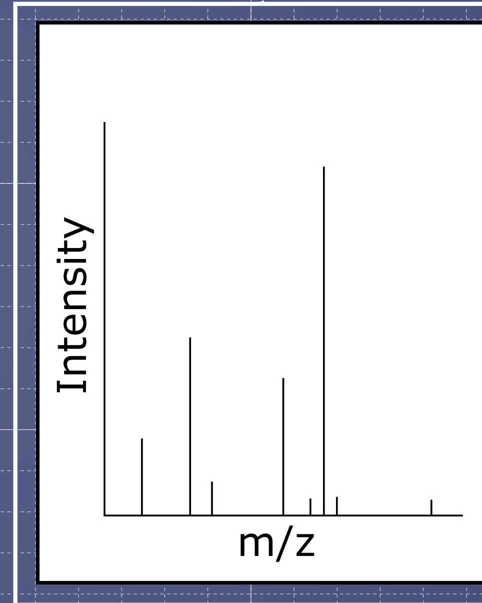
Despite all this, most scientists would probably agree that taking a step back and looking at the bigger picture can be essential to scientific progress, both for individuals and entire fields. In this talk, I will argue that scientists engaging with the philosophy of science will find that it encourages, facilitates and greatly enriches such broad scientific introspection. In a field as young and fast-moving as modern molecular biology, much could be gained from assimilating the philosopher's perspective into our scientific thinking.

Day 1 (afternoon): Data Management And Interpretation









Jean-Karim Hériché

EMBL Heidelberg
Heidelberg, Germany

Jean-Karim Hériché was trained as an engineer and obtained a PhD in biology from Université Joseph Fourier in Grenoble, France for work carried out at the French Atomic Energy Commission. He did post-doctoral research on cell cycle control during *Drosophila* development in Patrick O'Farrell's lab at the University of California, San Francisco and then moved to Richard Durbin's group at the Wellcome Trust Sanger Institute where he implemented bioinformatics tools and analysis methods for the MitoCheck project. He is now in the Cell Biology and Biophysics Unit at EMBL-Heidelberg where he works on image-based systems biology and bioimage informatics projects.

T6 Invited Speaker

Systems biology of mitosis: a data perspective

Hériché, Jean-Karim

EMBL Heidelberg, Germany

November 17th, 14:30

Mitosis is the dynamic process by which somatic cells segregate their chromosomes into daughter cells. We know that it requires tight coordination in space and time of the activities of many protein complexes. However, our knowledge of mitosis is incomplete and fragmented, giving oversimplified insights into disconnected aspects of the process. To address this issue, the MitoCheck and MitoSys projects have taken systematic and quantitative approaches to understand the roles, dynamics and interactions of hundreds of proteins involved in mitosis. I will discuss the role played by data and in particular data integration in these large, multidisciplinary projects.

Peter de Peinder

VibSpec
Utrecht, The Netherlands

Peter de Peinder studied Chemistry at Utrecht University and then became a member of the Vibrational Spectroscopy department as a junior scientist. In 1999 he got a position of a senior scientist at the Material Analysis department of Philips Research and from 2000-2004 a part-time scientist position at Utrecht University. In 2006 he left Philips Research Eindhoven and focused on his activities at VibSpec. In 2009 he obtained his PhD in chemistry on the characterisation of crude oils by a combination of spectroscopy and chemometrics. As a part-time member of the Inorganic Chemistry and Catalysis group of Utrecht University he is involved in *in-situ* vibrational spectroscopy of homogeneous and heterogeneous catalysts.

T7 Invited Speaker

Life is great but complex... like quantitative vibrational spectroscopy.

de Peinder, Peter

VibSpec, The Netherlands

November 17th, 16:45

Many industrial processes are already monitored by (Near)Infrared or Raman spectroscopy. Sometimes properties or concentrations are quantified based on these vibrational spectra even without exactly knowing where the information is hidden or where it is coming from. These are not theoretical models but empirical models based on multivariate data analysis or chemometrics. Even in relatively simple reactions where only a few chemical compounds are present this can be a difficult task and in general a reference method is needed for quantification. In biological systems it is clearly even more challenging. In many cases we are looking for minor changes in complex systems which makes it very important to realise which steps are necessary to create (semi) quantitative models based on molecular vibrations. The basics of vibrational spectroscopy and chemometrics will be explained to understand what the strengths and weaknesses are of these techniques. Simple matrices, e.g. a pharmaceutical tablet and more complex samples like crude oil, cow milk and glucose in blood will be used to demonstrate that the life of a vibrational spectroscopist is exciting (pun intended) but often complex.

T8 [P63] Short Talk

Towards quantitative 3D fluorescence microscopy with CoPS and array tomography

Yserentant, Klaus; Grußmayer; Kristin S., Hänselmann, Siegfried; Bierbaum, Sebastian; Schröder, Rasmus R.; Herten, Dirk-Peter

University of Heidelberg, Germany

November 17th, 17:30

A precise understanding of the detailed organizing principles in biological systems, requires quantitative information on appropriate spatial and temporal scales. Fluorescence microscopy is in principle able to provide such information *in situ*, with subcellular resolution and at single-molecule level allowing the determination of absolute molecule numbers even in complex environments. However, fluorescence microscopy relies on indirect observation of the molecular species of interest by detection of fluorophores as surrogate markers. To relate the observed fluorescence signal to absolute target molecule quantities, well-defined labeling schemes and a quantitative 3D imaging approach are essential. We are currently addressing these demands by employing a set of different techniques. First, we have developed a calibration probe to determine the degree of labeling on single-cell level for different self-labeling protein tags (e.g. SNAP-Tag or HaloTag) which allows to account for imperfect fluorescent labeling. Absolute counting of fluorophores is then achieved with our recently developed counting by photon statistics (CoPS) methodology which relies on the photon antibunching effect to infer the number of independent emitters in a diffraction-limited structure. For imaging of complex samples in 3D, we employ array tomography, i.e. physical sectioning of resin-embedded specimen and consecutive imaging of the resulting thin-sections. This approach avoids premature bleaching of out-of-focus fluorophores and reduces the encountered background signal. To ensure that fluorescent labels are retained during resin embedding, we exhaustively studied and optimized resin compositions as well as embedding protocols. In the future, we will combine quantitative labeling, counting by photon statistics and array tomography to accomplish unbiased absolute counting of target molecules in complex biological samples.

T9 [P20] Short Talk

Quantifying cellular robustness in genome-scale metabolic reconstructions

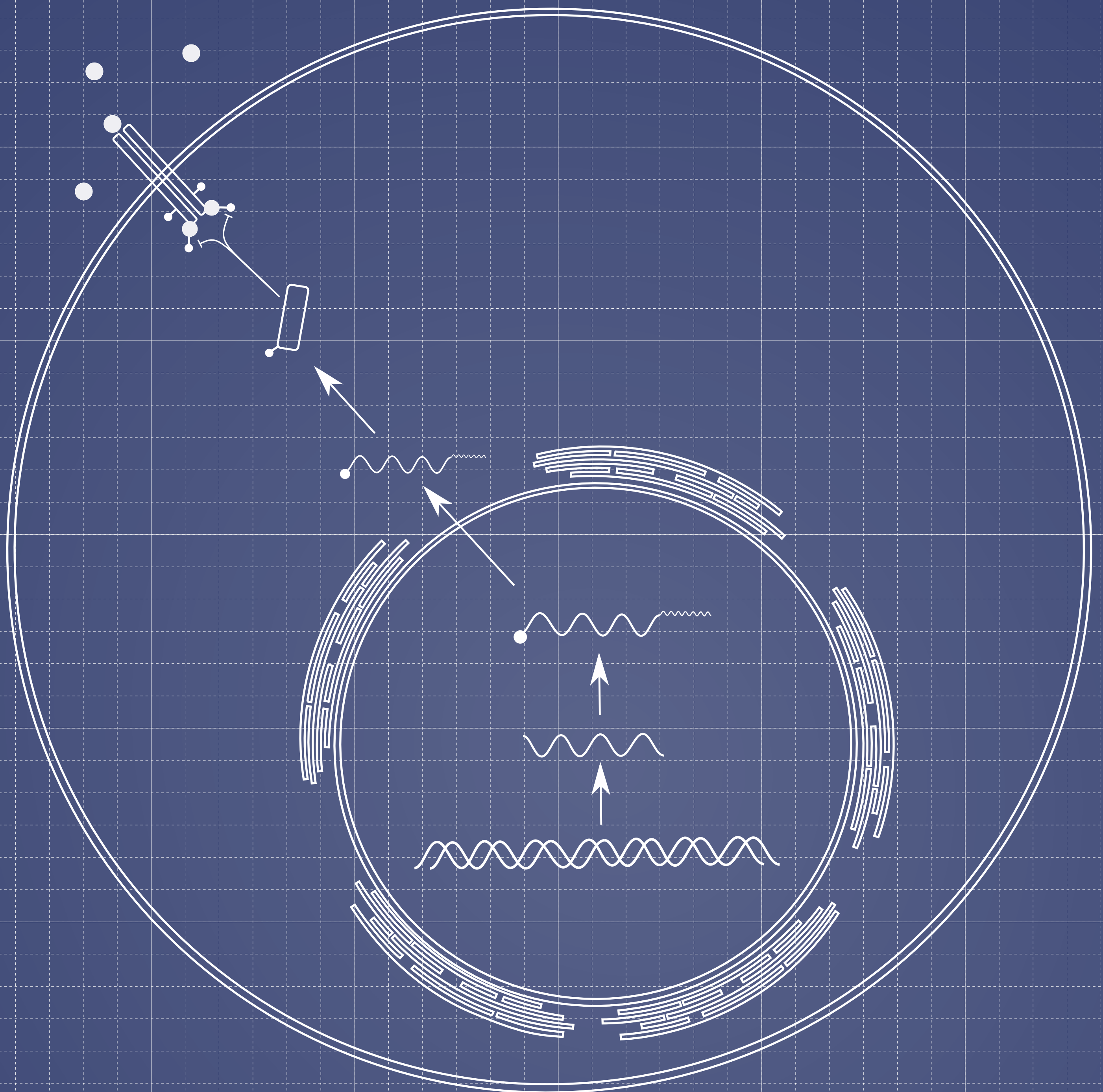
Galleguillos, Sarah Noel; Gerstl, Matthias P; Klamt, Steffen; Jungreuthmayer, Christian; Zanghellini, Jürgen

Austrian Centre of Industrial Biotechnology, Austria

November 17th, 17:45

Robustness, the ability of biological networks to uphold their functionality in spite of perturbations, is a key characteristic of all living systems. Although several theoretical approaches have been developed to formalize robustness, it still eludes an exact quantification. Here we present a rigorous and quantitative approach for the robustness of metabolic networks by measuring their ability to tolerate random reaction (or gene) knockouts. In analogy to reliability theory, based on an explicit consideration of all possible knockout sets, we exactly quantify the probability of failure for a given network function (e.g., growth). This measure can be computed if the network's minimal cut sets are known. We show that even in genome-scale metabolic networks the probability of (network) failure can be reliably estimated from minimal cut sets with lowest cardinalities. We demonstrate the applicability of our theory by analyzing the robustness of multiple *Enterobacteriaceae* and *Blattabacteriaceae* and show a dramatically low robustness for the latter. We find that robustness develops from the ability to proliferate in multiple growth environments consistent with experimentally found knowledge. The probability of (network) failure provides thus a reliable and easily computable measure of robustness and redundancy in (genome-scale) metabolic networks.

Day 2:
From Genome To Proteome



Luis Serrano

Centre for Genome Regulation
Barcelona, Spain

Dr Serrano graduated with a Bachelor's of Biological Sciences (1981) and Master's in Science (1982) from the Complutense University of Madrid. He then completed a PhD in Biochemistry in the Universidad Autónoma de Madrid (1985) and in Cell Biology at the Centro de Biología Molecular (CSIC-UAM) in 1987 and the University of Cambridge in 1991. Subsequently he spent 4 years in the laboratory of Professor A.R. Fehrs, at the Medical Research Council (MRC), UK, where he focused his research on protein folding. Currently Dr Serrano is the director of Centro de Regulación Genómica (CRG) and a member of the Spanish Society for Biochemistry and Molecular Biology (SEBBM), member of the European Molecular Biology Organisation (EMBO) and member of the Royal Spanish Academy of Sciences (Spain).

T10 EMBO Keynote Lecture

Transcriptome analysis of a small bacterium reveals non-TF predominant regulation which could be an ancient mode of responding to medium perturbations

Serrano, Luis

Centre for Genome Regulation, Spain

November 18th, 09:00

Determining the gene regulatory network is basic to have a global understanding of cell behavior. In general, studies of transcriptional regulation are limited to the annotated transcription factors (TFs), obviating other non-canonical regulators, or even unknown key players. Here, we describe the first systematic analysis of the protein-DNA interactome in a minimal bacterium, *Mycoplasma pneumoniae*. We have identified all potential DNA-binding proteins (DNABPs, 105 out of 689 annotated proteins) by DNA affinity chromatography, DNA pull-downs, and intact chromatin isolation. For each of them, together with some others added from the literature, we have determined their binding sites by ChIP-seq or biochemical assays. Also, we have studied the effect of overexpression and depletion of these putative DNA binding proteins by characterizing different *M. pneumoniae* strains using different 'omics' approaches. Strikingly, we found new moonlighting functions for highly conserved proteins, that show DNA binding properties as well as other activities, like proteases and metabolic enzymes. Interestingly, for the majority of the proteins analyzed, we found no transcriptome or growth phenotype upon overexpression (64.8%, 81 out of 125 proteins with both experiments). This is indicative of the robustness of the system, despite its simplicity. This integrative approach revealed that metabolic control is a key regulatory element, highlighting a non-TF factor layer of regulation in bacteria. This layer would include, but is not limited to, the role of supercoiling and the genomic context, the RNA structure, forming riboswitches or condition-dependent terminators, the RNA regulated decay, and the abundances of certain metabolites. This layer of non-TF regulation could represent an ancient way and be found in all organisms.

Leïla Perié

Institut Curie
Paris, France

Dr. Leïla Perié completed her PhD from the Cochin Institute, Paris in 2009. After that, she has worked on cell differentiation at College de France, National Cancer Institute in Amsterdam and Utrecht University. In 2015, she started a young research group at Curie Institute in Paris focussing on deciphering the hematopoietic tree using single cell lineage tracing methods in combination with mathematical modeling, as well as modeling T-cell dynamics. Apart from the intensive research in the field of quantitative immunology, Leïla is also providing training for scientists and promoting the use of scientific communication as a tool of empowerment.

T11 Invited Speaker

Deciphering the hematopoietic differentiation pathway at the single cell level

Perié, Leïla

Institut Curie, France

November 18th, 10:00

The immune system is composed of diverse, functionally distinct cell types that each contributes uniquely to immune responses. While the production of immune cells, a process called hematopoiesis, has been extensively studied, the structure of the differentiation pathways that produce the diversity of immune cell types during hematopoiesis remain poorly understood, especially in human due to technical restrictions.

Lineage tracing techniques, which track the descendant of individual cells, are powerful tools to quantitatively decipher the differentiation pathway when they are combined with computational approaches. My newly created lab at Curie Institute takes advantage of lineage tracing technics to study the hematopoietic differentiation pathway both in mice and human.

In this lecture, I will introduce technics of barcoding and discuss previous and new experimental results, as well as computational method for inference of the differentiation tree.

Leonie Ringrose

IRI Life Sciences
Berlin, Germany

Leonie Ringrose has been a professor since 2015 at the IRI for Life Sciences, Humboldt University, Berlin. From 2006 to 2014 she was a junior group leader at the Institute of Molecular Biotechnology (IMBA) in Vienna, Austria. In 2014 she visited the John Innes Centre, Norwich UK for a sabbatical in systems biology. Her group works on the epigenetic regulation in *Drosophila* and mouse development. They combine strategies of quantitative live imaging, mathematical modeling, computational approaches with molecular developmental biology to understand the interaction of the Polycomb and Trithorax proteins with their chromatin targets.

T12 Invited Speaker

"*In vivo* biochemistry": Absolute quantification and kinetic modelling applied to Polycomb and Trithorax regulation

Ringrose, Leonie

IRI Life Sciences, Germany

November 18th, 11:15

Absolute quantification of molecule numbers (how many molecules are there? Where are they?) and their kinetic properties (How long do they stay? How fast do they move?) opens the door to quantitative modelling. I will discuss methods for measuring these absolute values *in vivo* and show how we have combined this with quantitative kinetic modelling to gain new mechanistic insights into how the Polycomb and Trithorax group proteins interact with chromatin during the cell cycle in living *Drosophila*. This work has implications for our quantitative understanding of epigenetic memory and how it may be modulated in different contexts.

T13 Short Talk

Prediction of rare regulatory variants using deep learning

Urban, Lara

EMBL-EBI Cambridge, United Kingdom

November 18th, 12:00

Classical population genetics are based on quantitative trait loci (QTL) mapping that test for associations between polymorphic loci and molecular cellular traits like gene transcription and epigenetic modification. Although an abundance of QTLs have been identified, we are still lacking a comprehensive understanding of the regulatory impact of polymorphic genetic variants in the human genome. To address this challenge, I am developing an orthogonal approach that combines population-based QTL studies with sequence-based deep learning approaches. Deep models capture hierarchical and complex patterns in genomic sequence and can detect genetic variants which are predictive for changes in molecular traits. At present, I am applying these approaches to model the genetic component of histone variation in human monocytes. Uniquely, using datasets from BluePrint, I have access to ChIP-Seq data from ~200 individuals, which allows to directly compare and combine population- and sequence-based predictions. The aim of these approaches is to interpret rare variant mutations, which will provide important insights into large disease cohorts available through resources like UK Biobank.

John Liebler

The Art of the Cell
Guilford, United States of America

As a former Lead Medical Animator of XVIVO Scientific Animation, John Liebler is best known for his work with Harvard University/Biovisions on the pivotal molecular movie “The Inner Life of the Cell”. He has over 20 years of experience creating scientific images and interactive 3D videos for a wide range of pharmaceutical, biomedical and educational companies. From science animation videos used to explain cell biology to students to scientific method animations clarifying the research of pioneers in the field of biosciences. John’s biomedical animations educate and inspire audiences of all backgrounds and interests across the globe.

T14 Invited Speaker

OK, but what does it look like?

A discussion of how scientific data informs art, and how artistic concerns can inform scientific research, as well as how those two disciplines can be at odds with one another.

Liebler, John

The Art of the Cell, United States of America

November 18th, 13:45

For as long as humans have existed, we have been using visual art as way to explore and understand the world around us, and that art has inspired those that followed to explore further. The early scientists: Copernicus, DaVinci, Galileo, were artists, creating drawings and paintings to record their observations of the world.

While working on "The Inner Life of the Cell" back in 2004, Dr. Alain Viel would send me text heavy scientific papers about the molecular structures and interactions he wanted me to animate. I would scan through them quickly for any visual information, i.e. I looked at the pictures first. If there were no pictures, and I would email back and ask: "OK, but what does it look like?" Then I realized that it was my job to figure that out. I learned to use pdb structures to build models that I could turn around and see from all angles, and my understanding of the molecular world began to open up.

Just as I was able to access the science by making art, I think that researchers might benefit from trying to make art from their research. Presenting data in a visual or even tactile way allows access to parts of the brain which can't be reached by language or numbers alone, even if only in an intuitive way. Artistic or even aesthetic questions may lead to lines of inquiry that have not been explored.

My molecular art is based on scientifically derived data, but it is not "real". It is just an abstraction of that data, simplified and presented to convey a message. Often the data is chaotic or incomplete, and the job of the artist is to find order in the chaos to clarify the message. Sometimes the chaos is the message. Art is a series of decisions made by the artist. What to leave in, what to take out. Being informed by data still involves choice. Communication or miscommunication can be the result, and although care must be taken to avoid miscommunication, the benefits of aesthetic visualization outweigh the risk. Art makes science accessible to non scientists such as students and the general public, which raises awareness of scientific concerns among the general public and inspires students to become the next generation of scientists.

T15 Short Talk

Breaking the genetic code: Multiple reassignments of the codon CUG during yeast evolution

Krassowski, Tadek

University College Dublin, Ireland

November 18th, 14:30

The genetic code (translation table of codons into amino acids) is almost universal. However, there is a clade of yeasts, including the major human pathogen *Candida albicans*, which has been known for almost 30 years to translate CUG as serine instead of leucine. Until recently this was the only known reassignment of a sense codon in the nuclear genome of any eukaryote, but in 2016 *Pachysolen tannophilus*, a yeast species that is phylogenetically sister to the CUG-Ser clade, was discovered to translate CUG as alanine. We systematically examined about 50 yeast genomes in the subphylum *Saccharomycotina*, in order to discover the phylogenetic extents of the CUG-Ala and CUG-Ser clades, and to look for additional genetic code changes. First, we used a bioinformatics approach with multi-species alignments to predict how CUG is translated in each species. Then, for 19 selected species, we validated their genetic codes by peptide sequencing. We discovered that multiple reassignments of the CUG codon to Ala and Ser have occurred in closely related clades. We hypothesise that these changes were caused by an initial ‘catastrophe’ in which the single tRNA gene that translated CUG was either lost or damaged in the common ancestor of these clades. We are currently testing this hypothesis by phylogenetically examining CUG-decoding tRNA genes. We are also designing experiments to push a yeast species to artificially change its genetic code. These experiments will give insight into the evolutionary mechanism of genetic code change in the *C. albicans* clade, and may produce new tools for genetic manipulation of *C. albicans* and related pathogens. They may also shed some light on how genetic code changes affect pathogenicity.

Paola Picotti

Department of Biochemistry, ETH Zürich
Zürich, Switzerland

Professor Paola Picotti obtained her PhD from the University of Padova. In 2006, she joined Professor Ruedi Aebersold's group at ETH Zurich, where her research received the ETH Latsis Prize 2011. At the beginning of 2011, she started her own research group and was appointed assistant professor at the Institute of Biochemistry at ETH Zurich. Her team focuses on the study of the effects of intracellular protein misfolding and aggregation using novel proteomics approaches. Among her pioneering achievements is the development of a method to analyze protein structural changes in biological samples and on large scale. In 2015 she was selected as an EMBO Young Investigator, while recently she won the 2016 Robert J. Cotter new investigator award for her significant contribution in the field of proteomics.

T16 EMBO Young Investigator Lecture

Monitoring protein structural changes on a large scale

Picotti, Paola

Department of Biochemistry, ETH Zürich, Switzerland

November 18th, 16:15

Protein aggregation diseases are associated with the intracellular accumulation of aggregates of specific misfolded proteins. Aggregation-prone proteins (APPs) are characterized by a variety of seemingly unrelated sequences, functions and localizations, but upon misfolding they adopt very similar structures, that share the so-called amyloid fold. These structures have been associated to cellular toxicity and cell degeneration. Recent genetic screens uncovered sets of genes that significantly reduce the toxicity of each APP and are conserved from yeast to higher organisms. These modulators are very promising for therapeutic purposes, but their mechanisms of action is currently unknown. We applied a strategy based on unbiased and targeted proteomic analyses to a set of yeast models of APP toxicity with the purpose of characterizing cellular responses to different APPs and identifying mechanism of action of known toxicity modulators. We selected a set of markers for the activation state of 200 pathways and biological processes in yeast and designed a targeted proteomic assay that measures such markers in about 1 hour. We used the assay to analyze how cells respond to APP toxicity and determine which cellular processes or pathways each genetic modulator rewires or activates to compensate for the toxic insult. Such an assay can probe multiple pathological features at the same time and has potential for drug screening and for the elucidation of enigmatic mechanisms of action. In order to relate the observed cellular effects to the specific structural states produced along the aggregation process of each APP, we developed a novel mass spectrometric tool to quantitatively analyze the conformational changes of amyloid-forming proteins directly in their cellular environment. I will show how this approach could be used to analyze protein conformational changes such as those associated to allosteric regulation, receptor activation or amyloid formation, *in vivo* and on a global scale.

T17 [P58] Short Talk

An engineering approach to molecular assembly of the Type 3 Secretion System

Tuckwell, Andrew

EMBL Australia UNSW, Australia

November 18th, 17:00

The Type 3 Secretion System (T3SS) is a megadalton-scale bacterial organelle functioning as a molecular syringe that injects proteins directly into eukaryotic cells. Several important pathogens utilise this system as a virulence factor. As it features a surface-presenting needle tip complex, the T3SS is an attractive candidate as a therapeutic target. The massive, multi-component structure of the T3SS, and its all-or-nothing assembly presents both challenges to its study and opportunities to our understanding of how molecular interactions can scale. A developing approach in structural biology is use of hybrid methodologies; integration of data from several techniques such as CryoEM, solution scattering and single molecule microscopy. In concert, several techniques can achieve a richer model of the dynamics and structures of large and complex molecular assemblies. Complementing this theme, we employ an engineering approach to understanding molecular structres; by re-building biological complexes from the bottom up and probing assembly structure and kinetics in the process.Integrating current structural knowledge, we form a 'biological blueprint' of the T3SS tip complex. Using DNA nanotechnology, we design and synthesize molecular scaffolds to direct the arrangement and stoichiometry of protein subunits as is laid out in the blueprint. Here we present the kinetics of T3SS tip complex proteins assembling on DNA scaffolds, as well as TEM and solution X-ray scattering structures of assembly components. By assembling sub-complexes *in vitro*, the context of subunits *in-situ* can be retained whilst permitting measurements of structure and kinetics previously confounded by the distant whole. The precise control afforded by DNA nanotechnology also expands the scope of assembly manipulation. Thus, in studying the nature of large molecular machines, we may broaden the range of both samples and sample variables, as well as how we measure them.

T18 Short Talk

Dynamic measurement if kinase activity in live single cell

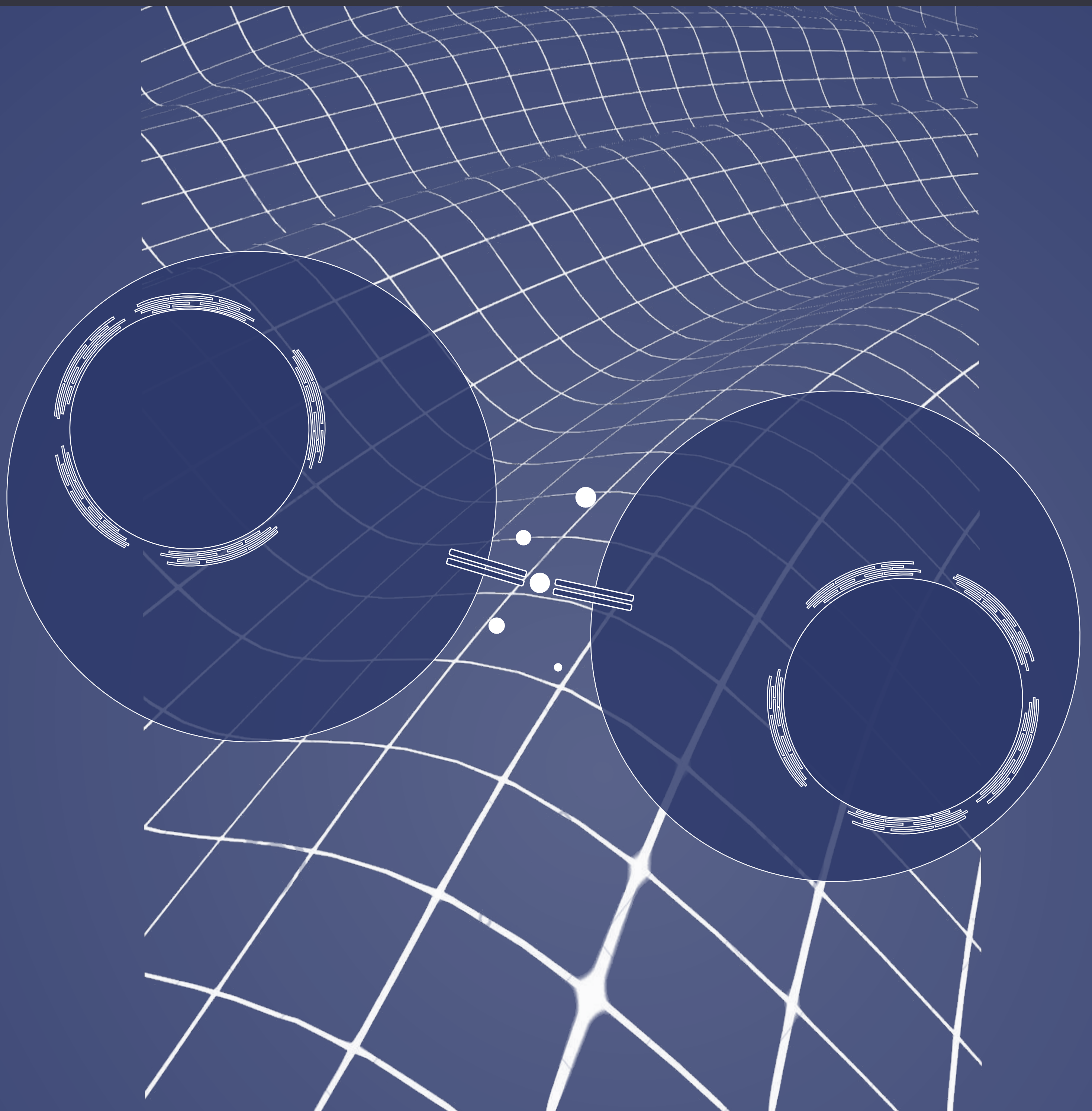
Durandau, Éric; Ma, Min; Aymoz, Delphine; Pelet, Serge

Université de Lausanne, Switzerland

November 18th, 17:15

The phosphorylation of signaling cascade components is a key post-translational modification used in signal transduction. Although all kinases catalyze this biochemical reaction, each individual kinase possesses its specific pool of substrates. Moreover, the temporal activity of these enzymes varies from cell to cell depending on intra- or extracellular cues. Knowing that kinase mis-regulation is implicated in many diseases, such as cancer, it becomes crucial to quantify the heterogeneity of the dynamic kinase activity at the single cell level. Microscopy is an ideal technique for such investigation. However, fluorescent assays have to be established to quantify this enzymatic activity in living cells. Using a synthetic biology approach, we designed a fluorescent biosensor that undergoes nuclear-to-cytoplasmic relocation upon phosphorylation by the kinase of interest. Combination of time-lapse microscopy measurements and automated image analysis allows the quantification of the dynamics of kinase activity in hundreds of single cells. As proof of concept, we generated a Synthetic Kinase Activity Relocation Sensor (SKARS) for Mitogen Activated Protein Kinases (MAPK) of the mating pathway in *S. cerevisiae.* The kinetics of the MAPK activation exhibits a large heterogeneity between single cells due to an inhibition of signal transduction at specific stages of the cell-cycle. With our quantitative and dynamic assay at the single cell level, we revisit the cross-inhibition between the cell-cycle and the mating pathway activation.

Day 3:
Cell Communication Shaping Tissues



Raymond E. Goldstein

Department of Applied Mathematics and Theoretical Physics, University of Cambridge
Cambridge, United Kingdom

Professor Goldstein graduated from the Massachusetts Institute of Technology (MIT) with a double-major Bachelor of Science degrees in Physics and Chemistry in 1983. He continued his education at Cornell University, where he was awarded a Master of Science degree in Physics in 1986, followed by a PhD in 1988 for research on phase transitions and critical phenomena supervised by Neil Ashcroft. Professor Goldstein is a Fellow of the American Physical Society, the Institute of Physics, the Institute of Mathematics and its Applications, and the Royal Society. He is currently a Schlumberger Professor of Complex Physical Systems at University of Cambridge, focusing his research on non-equilibrium biological systems.

T19 Keynote Lecture

Upside Down and Inside Out: The biomechanics of cell sheet folding

Goldstein, Raymond E.

Department of Applied Mathematics and Theoretical Physics, University of Cambridge, United Kingdom

November 19th, 09:00

Deformations of cell sheets are ubiquitous in early animal development, often arising from a complex and poorly understood interplay of cell shape changes, division, and migration. In this talk I will describe an approach to understanding such problems based on perhaps the simplest example of cell sheet folding: the “inversion” process of the algal genus *Volvox*, during which spherical embryos literally turn themselves inside out through a process hypothesized to arise from cell shape changes alone. Through a combination of light sheet microscopy and elasticity theory a quantitative understanding of this process is now emerging.

Dagmar Iber

Department of Biosystems Science and Engineering, ETH Zürich
Zürich, Switzerland

Dagmar Iber studied mathematics and biochemistry in Regensburg, Cambridge and Oxford. She holds Master degrees and PhDs in both disciplines. After three years as a Junior Research Fellow in St John's College, Oxford Dagmar became a lecturer in Applied Mathematics at Imperial College London. Dagmar has joined ETH Zürich in 2008 after returning from an investment bank where she worked as an oil option trader for one year. Professor Iber's group develops data-based, predictive models to understand the spatio-temporal dynamics of signaling networks. Her recent work focuses on mouse organogenesis and patterning systems to further understand the control of organ growth and robustness of signalling mechanisms in response to evolutionary changes.

T20 Invited Speaker

From Networks to Function – Computational models of organogenesis

Iber, Dagmar

Department of Biosystems Science and Engineering, ETH Zürich, Switzerland

November 19th, 10:00

One of the major challenges in biology concerns the integration of data across length and time scales into a consistent framework: how do macroscopic properties and functionalities arise from the molecular regulatory networks and how do they evolve? Morphogenesis provides an excellent model system to study how simple molecular networks robustly control complex pattern forming processes on the macroscopic scale in spite of molecular noise, and how important functional variants can evolve from small genetic changes. Recent advances in 3D imaging technologies, computer algorithms, and computer power now allow us to develop and analyse increasingly realistic models of biological control. In my talk, I will show how data-based modelling can be used to define mechanisms for fundamental developmental processes and I will discuss the computational challenges that arise.

Irene Miguel-Aliaga

Imperial College London
London, United Kingdom

Irene Miguel-Aliaga is Professor of Genetics and Physiology at Imperial College London and Programme Leader at the London MRC Clinical Sciences Centre. She obtained her DPhil in Genetics from the University of Oxford, and explored how neurons acquire their identity during postdoctoral work at Harvard, Linkoping University and NIMR (now Crick Institute), London. First at Cambridge and now in London, her research group is investigating cellular and organ plasticity and exploring the mechanisms by which organs sense change and respond to it. Their work has primarily focused on the fly intestine and its neurons, investigating the links between gut neural system, reproduction and metabolic adaptation processes. Irene was elected to the EMBO YIP programme in 2012 and is the recipient of an ERC Starting Grant.

T21 Invited Speaker

Homeostatic Plasticity

Miguel-Aliaga, Irene

Imperial College London , United Kingdom

November 19th, 11:15

Internal organs are constantly exchanging signals, and can undergo profound anatomical and functional changes in response to them, even in fully developed organisms. Such organ plasticity results from a need to integrate and respond to both environmental information and internal state, and is key to maintaining homeostasis and driving adaptive changes. We are interested in understanding the mechanisms by which organs sense change and respond to it: the molecules, cellular events and physiological adaptations involved. The intestine and its neurons are a fantastic system with which to tackle these questions. Over the past few years, we have initiated the characterization of enteric neurons in *Drosophila melanogaster*, and have developed new technology for the study of their functions (1). Our investigations have uncovered evolutionarily conserved mechanisms of autonomic control (1,2), and have also characterized a novel and physiologically relevant mechanism, reminiscent of neurovascular interactions in mammals, which points to a key role for the intestinal vasculature in adaptations to malnutrition (3).

More recently, we have begun to explore the physiological plasticity of the intestinal epithelium - an obvious cellular target of the enteric neurons – both transcriptionally and metabolically. I will present some of this work, which has revealed unexpected sexual dimorphisms and intestinal contributions to reproductive success (4,5). I will also discuss some of our current work, aimed at 1) exploring the existence of cell-intrinsic sex differences in other fly cell types, mice and human cells, and 2) establishing their significance in the context of cell plasticity and commitment.

1 Cognigni P, Bailey AP, Miguel-Aliaga I (2011) Enteric neurons and systemic signals couple nutritional and reproductive status with intestinal homeostasis. Cell Metab 13(1):92-104.

2 Talsma AD, Christov CP, Terriente-Felix A, Linneweber GA, Perea D, Wayland M, Shafer OT, Miguel-Aliaga I (2012) Remote control of renal physiology by the intestinal neuropeptide pigment-dispersing factor in *Drosophila*. Proc Natl Acad Sci U S A 109(30):12177-82.

3 Linneweber GA, Jacobson J, Busch KE, Hudry B, Christov CP, Dormann D, Yuan M, Otani T, Knust E, de Bono M, Miguel-Aliaga I (2014) Neuronal control of metabolism through nutrient-dependent modulation of tracheal branching. Cell 16;156(1-2):69-83.

4 Reiff T, Jacobson J, Cognigni P, Antonello Z, Ballesta E, Tan KJ, Yew JY, Dominguez M, Miguel-Aliaga I (2015) Endocrine remodelling of the adult intestine sustains reproduction in *Drosophila*. eLife 4:e06930.

5 Hudry B, Khadayate S, Miguel-Aliaga I (2016) The sexual identity of adult intestinal stem cells controls organ size and plasticity. Nature 530(7590):344-8.

T22 [P57] Short Talk

How tissues coordinate growth in an organ: Insights from modeling clonal lineages in fish

Tsingos, Erika; Höckendorf, Burkhard; Sütterlin, Thomas; Kirchmaier, Stephan; Centanin, Lázaro; Grabe, Niels; Wittbrodt, Joachim

Centre for Organismal Studies, University of Heidelberg, Germany

November 19th, 12:00

The continuously growing eye of fish presents the perfect model system to explore how different tissues coordinate proliferation in an organ. The neural retina and surrounding retinal pigmented epithelium (RPE) share a bipartite stem cell niche. Strikingly, labeling the progeny of individual stem cells in medaka fish (*Oryzias latipes*) reveals heterogeneous lineages that differ between neural retina and RPE. Why do these tissues grow differently, and how can heterogeneous lineages be reconciled with homogeneous organ growth? To answer these questions, we simulate a 3D virtual eye in a computational cell-based model implemented in the platform EPISIM. In the virtual eye, a monolayer of spherical cells is affixed to an expanding hemispherical surface. Cells only proliferate within a narrow ring at the base of the hemisphere; divisions occur with a random chance. This simple model shows that the distinct clonal pattern of neural retina and RPE results from different growth modes. While cells in the RPE passively proliferate in response to an expanding scaffold, the neural retinal cells control organ growth pace. Moreover, neural retinal stem cells *in vivo* preferentially choose a biased division axis that hints at a role in regulating eye shape. By exploring various proliferation and growth modes, the model highlights a role of the retina in controlling eye growth, eye shape, and retinal architecture. By tweaking these parameters, evolution can calibrate the eye to perfectly adapt to the animal's ecological niche.

Russ Hodge

Max Delbrück Center for Molecular Medicine
Berlin, Germany

Russ Hodge is currently working as a science writer at the Max Delbrück Center for Molecular Medicine in Berlin, Germany. His latest book is The Case of the Short-fingered Musketeer, about a 20-year search for the causes of essential hypertension. Previously he ran the Office of Information and Public Affairs at the European Molecular Biology Laboratory in Heidelberg, where he was heavily involved in science education. He was instrumental in writing the grants that established the science teaching magazine 'Science in School', the European Learning Laboratory for the Life Sciences at EMBL, and the international Science on Stage project. His work involves writing stories about science for the general public and more specialized audiences, creating new teaching materials for workshops, helping scientists develop their communication skills, and helping institutes improve their communication, outreach and education activities.

T23 Invited Speaker

How to see a ghost, think like a molecule and write like a scientist

A new model of the relationship between science and communication, and what it means for teaching and research

Hodge, Russ

Max Delbrück Center for Molecular Medicine, Germany

November 19th, 13:45

Most scientists see communication pragmatically: as a way of presenting their work to their peers and other audiences, to gain funding and other types of support. Communication is so important to the major milestones of a career that most researchers have recognized the value of learning to do it well. But communication and research are connected at a more profound level: distilling ideas into texts, images, mathematics or another representational system is an essential step in structuring thinking. The connection lies in the complex models that give everything in science its meaning. Models are intricate cognitive architectures that individual scientists build in their minds and constantly revise through learning and experience. As they do so, they integrate concepts about specific systems into larger theories such as evolution, the fundamental principles of science, and basic cognitive patterns that we use in our daily lives. This process is crucial to success, but it is poorly understood and rarely discussed in any systematic way during a scientist's education.

Communicative situations expose the structure and invisible architecture of a model by making the connections between ideas explicit, so that scientists can check their logical consistency, discover hidden assumptions and patterns, apply new ones and generate new scientific questions. These are usually important steps along the way to new discoveries. This makes the process of communication fundamental to the lifelong process of learning that is necessary for a successful career in science. In this talk I will show how communicative tools can be applied to the "mental game" of science to help scientists improve both their writing and their research.

T24 Short Talk

Myc transcription factors regulate mouse lens development and eye organogenesis

Cavalheiro, Gabriel; Rodrigues, Gabriel; Gomes, Anielle; Martins, Rodrigo; Zhao, Yilin; Cvekl, Ales

EMBL Heidelberg, Germany

November 19th, 14:30

Myc transcription factors regulate cell proliferation, growth and differentiation in various developing tissues, and their deregulation may lead to tumorigenesis or developmental malformations. The lens is composed of proliferative epithelial progenitor cells that after cell cycle exit undergo terminal differentiation to form fiber cells. One key aspect of the differentiation of these fiber cells is the degradation of their organelles, including the nuclei (denucleation) resulting in a fully transparent organelle-free zone (OFZ) in the center of the lens. Nuclei degradation requires low levels of p27Kip1 expression and high Cdk1 activity in post-mitotic fiber cells to dismantle the nuclear envelope, and DNase II-beta activity for DNA degradation. Previously, we demonstrated that c-myc is required for cell proliferation in the developing lens, but not for OFZ formation. Targeted deletion of N-myc from mouse lens progenitors resulted in eye and lens growth impairment. Interestingly, we observed that N-myc inactivation did not affect cell proliferation or survival in embryonic lens. Remarkably, N-myc-inactivated lenses present a delay to form an OFZ, since their terminally differentiating fiber cells retain the nucleus for longer than control lenses. This is associated with decreased DNase II-beta expression. The remnant nuclei failed to decrease p27Kip1 expression, suggesting that Cdk1 activity may be downregulated in N-myc-inactivated lens fiber cells. Furthermore, simultaneous inactivation of N-myc and c-myc dramatically reduced eye and lens volume and also failed to form an OFZ. Our findings suggest that Myc transcription factors regulate distinct cellular events during lens development *in vivo*. These data contribute to a better comprehension of the molecular mechanisms that control of organelle degradation in the lens, and constitute a previously undescribed function for the N-myc proto-oncogene.

Timothy A. Ryan

Weill Cornell Medical College
New York, United States of America

Dr. Ryan received his Bachelor of Science in Physics at McGill University and his PhD in Physics at Cornell in the laboratory of Watt Webb. After carrying out postdoctoral work at Stanford Medical School he started his own group at Weill Cornell Medical College, USA where he is currently a Tri-Institutional Professor. The focus of his lab is on the molecular basis of synaptic transmission in mammalian brain. His prime interest lies in understanding the regulation of presynaptic strength. Dr Ryan's group uses biophysical tools to measure physiological parameters at synapses, including exocytosis, endocytosis, action potential waveforms and voltage-triggered calcium fluxes in individual presynaptic boutons. Dr Ryan's team develops state-of-the-art optical methods to obtain a quantitative understanding of presynaptic function and attempts to reduce the complexities of synaptic transmission in a physico-chemical framework.

T25 Invited Speaker

Power supplies for brain cells: the cost of thinking

Ryan, Timothy A.

Weill Cornell Medical College, United States of America

November 19th, 15:15

The brain is a highly demanding machine from the point of view of metabolism consuming 20% of available fuel in the body while representing only 5% of the mass. Additionally the brain is highly vulnerable to acute metabolic restriction, since interruptions in fuel availability leads to rapid comprise in brain function. We have been carrying out experiments to understand quantitatively how synapses, the major control point of information flow between brain cells, rely on and maintain adequate supplies of fuel. To carry this out we designed a novel analytical optical approach that allowed us to measure the concentration of ATP inside living synapses. Experiments using this probe has revealed a strong regulatory system in place at nerve terminals that relies on both feedback and feedforward biochemical circuits that adjust the production of ATP locally to meet energetic needs of synapse function. I will be discussing both our published work and our recent efforts to understand the molecular basis of the regulatory biochemical circuitry.

T26 Short Talk

Mapping the distribution of chemokines in lymphoid tissues: Combining super-resolution imaging with multiscale modelling

Cosgrove, Jason; Miller, Helen; Butler, James; Jarrett, Simon; O Toole, Peter; Stein, Jens; Leake, Mark; Timmis, Jon; Coles, Mark

University of York, United Kingdom

November 19th, 16:00

Chemokines are small molecules that regulate the migration of immune cells. Due to a complex regulatory network occurring across molecular, cellular and tissue levels of organisation it has yet to be determined how these molecules form functional gradients within complex microenvironments. To address this issue we have measured the diffusion constant of CXCL13 and CCL19 and simulated CXCL13 gradient formation and associated B-cell responses using a 3D multiscale model of a primary lymph node follicle. Measurements of diffusion constants were performed using single-molecule super-resolution fluorescence microscopy on Alexa647-labelled chemokines in collagen matrix. Results suggest that the Einstein-Stokes relation is likely to over-estimate the diffusivity of chemokines *in vivo* as it does not take the biochemistry of the molecule, or the complexity of the local environment into account. These measures, with additional imaging and cytometry data, were used to parameterise a multiscale model, which was implemented using acceptance test-driven development. *In silico* migration was consistent with *in vivo* datasets, with no statistically significant difference detected for either wild-type or CXCR5-/- B-cells. *In silico* CXCR5 expression on the cell surface is location-dependent with complete loss of the receptor leading to a reduced scanning capacity. Simulations of gradient formation suggest that chemokine fields within the follicle are nonuniform and identify the CXCL13 diffusion constant, secretion rate and decay rate as key parameters governing the efficacy of B-cell scanning. This result suggests that the microanatomical distribution of chemokine, and not just absolute concentration, is a key determinant of efficacy. Taken in concert, this combined experimental and theoretical approach has permitted the consolidation of data across spatiotemporal scales into an executable software platform used to examine chemokine gradient formation in lymphoid tissues.

T27 Short Talk

Growth and form in 4th Dimension: Non- invasive, *in vivo* quantification of growth anatomy and morphology through time

Singh, Amit; Fleddermann, Roland; Huang, Keshu; Lee, Woei Ming; Nicotra, Adrienne; Chow, Jong H

Australian National University, Australia

November 19th, 16:15

The formation of multicellular organisms is a dynamic process, a progressive play of cells regulated by physical and evolutionary forces develop intriguing and presumably, optimized functional structures. A robust quantitative understanding of organ level growth dynamics is essential to understand how growth leads to a characteristic functional form. Here, we develop a multimodality imaging technique by combining time domain - optical interferometry with multi view stereo imaging method to non-invasively obtain fast three dimensional, volumetric reconstruction of anatomical developments and shape transitions of growing *Arabidopsis thaliana* leaves. We quantify the relative growth dynamics of venation network vs the leaf lamina and quantify how the expansion of a filament and elastic sheet would influence the overall shape of the system. We report the local growth rates, dynamic shape confirmation of leaf at different stages of growth. *Arabidopsis* rosette shows change in elevation angle as a result of circadian regulation; our multi modal technique also allows us to measure overall pattern and magnitude of leaf movement, *in-vivo* under different light conditions. We aim to develop a coherent understanding of the mechanistic basis of integration of vasculature with leaf shape and how multitude of venation patterns and leaf shapes are developed in nature.

Posters

Poster sessions will take place as follows (for more information see page 146):
Thursday, 17th November, 15:45-16:45, Helix A
Friday, 18th November, 15:15-16:15, Helix A

P1 **Albury, Cassie**
Utilising the benefits of whole exome sequencing to advance efforts in Familial Hemiplegic Migraine diagnostics

P2 **Amande, Tivkaa**
Degradation of volatile hydrocarbons in estuarine environments

P3 **Argelaguet, Ricard**
Group Factor Analysis to disentangle common and specific sources of variation between different biological layers

P4 **Balázs, Zsolt**
Long-read sequencing analysis of the dynamic transcriptome of the Pseudorabies *virus*

P5 **Bartels, Kim**
Crystallization of the inner membrane protein SbmA from Escherichia coli

P6 **Becker, Kolja**
Reverse Engineering EMT

P7 **Beckers, Maximilian**
Quantitative structural information from single molecule FRET

P8 **Bobonis, Jacob**
Origin, functional diversification and substrate specificity determinants in the family of NCS1/FUR transporters

P9 **Boissonnet, Tom**
Interactions between astrocytes and synapses in a rat animal model of epilepsy

P10 **Boucher, Matthew**
SMC4 is essential for sporozoite formation in the Malaria parasite

P11 **Bradshaw, William**
Age-dependent changes in the expressed immunoglobulin repertoire of a short-lived teleost

P12	**Caruana, Nikeisha** *A slimy situation: Using ‘omics and computational tools to understand the biochemical and biophysical properties of* Sepiadariid *slime.*
P13	**Chheda, Himanshu** *Whole genome view of the consequences of a population bottleneck using 2926 genome sequences from Finland and United Kingdom*
P14	**Crosskey, Tom** *Investigating the folding and insertion of bacterial outer membrane proteins by atomic force microscopy*
P15	**Czuchnowski, Jakub** *A semi* in vivo *system for PML body research*
P16 T2	**Dahl-Jensen, Svend** *Deconstructing the formation of the ductal network in the pancreas*
P17	**Dönertas, Handan Melike** *Ageing-related changes include increase in interaction entropy*
P18	**Duenas, Corina** *Granulomatosis with Polyangiitis: Knowledge integration and network analysis towards mechanistic understanding of underlying pathogenesis*
P19	**Duong, Nguyet** *Gel-free mass spectrometry to explore the thiol proteome of chronic diseases*
P20 T9	**Galleguillos, Sarah Noel** *Quantifying cellular robustness in genome-scale metabolic reconstructions*
P21	**Golushko, Ivan** *Membrane-mediated interaction of curvature-active proteins*
P22	**Guerra, Matteo** *A new drug discovery platform based on Bioluminescence Resonance Energy Transfer: bacterial interaction ß’-s70 interfering compounds identification*
P23	**Harsh, Moshir** *Theoretical models for nuclear pore complex assembly*
P24	**Hassan, Shabbeer** *How to phase genomic data with indels? A comparative study*
P25	**Hollmann, Nele** *The Notch1 trimeric transcription factor complex regulates HEY1 in a cooperative manner*

P26 **Jann, Cosimo**
Analyzing growth and carboplatin sensitivity of ovarian cancer cells in 3D cell culture using confocal microscopy

P27 **Jarrett, Simon**
Methods for simulating molecule diffusion for agent-based in silico *models of biological systems*

P28 **Juyoux, Pauline**
Targeting Bax transmembrane domain oligomerisation

P29 **Kantamneni, Sravya M.**
Conformational sampling using genetic algorithm and its comparative analysis with respect to systematic search

P30 **Kennouche, Paul**
Deep mutagenesis and functional analysis of the pilin protein from Neisseria meningitidis

P31 **Kentepozidou, Elissavet**
Development of a bioinformatics tool for de novo *identification of microRNAs*

P32 **Kojic, Ana**
Characterization of muscle regulator ANKRD1 in glioblastoma cell lines U87-MG and LN229

P33 **Kommer, Christoph**
A parametrized correlation measure model for enhancer-gene network inference in T cells

P34 **Körber, Verena**
Dynamic modeling of tumor initiation and progression

P35 **Lenzen, Benjamin**
Ribonomics of abundant chloroplast RNA binding proteins

P36 **Liu, Liyan**
Modelling lymphocyte proliferation on the single cell level based on data from time lapse fluorescence microscopy

P37 **Maistrenko, Oleksandr**
Variation in core and accessory genome of Escherichia coli *isolated from soil from riparian areas in New York State*

P38 **Milioli, Heloisa**
Pairwise biomarker combinations and predictive modelling for breast cancer intrinsic subtypes

P39 **Morgunov, Alexey**
Investigating residue coevolution in proteins from a structural perspective

P40 **Muskovic, Walter N.**
Utilising whole-transcriptome time-series data to unravel microRNA regulatory networks

P41 **Pažický, Samuel**
Studies of NKp30 oligomerization and ligand binding

P42 **Peña Navarro, David Alejandro**
Metabolomics based pathway thermodynamics

P43 **Perron, Umberto**
In silico *prediction of lncRNA function using tissue specific and evolutionary conserved expression*

P44 **Ponzi, Erica**
Extending the simulation extrapolation (SIMEX) technique to pedigree reconstruction - a statistical method meets quantitative genetics

P45 **Puga, David E.**
The role of Evx in the locomotion of Platynereis dumerilii *and its implication for* Urbilateria

P46 **Ramirez-Santiago, Guillermo**
A kinetic model for chemical neurotransmission

P47 **Ravikumar, Balaguru**
Promiscuity of kinase superfamily as an effective platform for lead molecule screening

P48 **Rojas Cordova, Carlos**
Crystallization Screening of various Impß-H1-Imp7 constructs

P49 **Sakson, Roman**
Establishment of an MRM assay for the quantification of human Hsp90 and its cochaperones

P50 **Sammour, Denis**
Scores for standardization of on-tissue digestion of formalin-fixed paraffin-embedded tissue in MALDI-MS imaging

P51 **Sauer, Jan**
Deep learning to detect organoids

P52 **Schienstock, Dominik**
Cell and nuclear packing during tissue growth

P53 **Silva, Patrícia M.**
Temporal and spatial control of fungal filamentous growth

P54 **Sitarska, Ewa**
The secrets of Munc18 interactions

P55 **Suckale, Jakob**
Making nanoscale numbers tangible with 3D printing

P56 **Tan, Winnie**
Discrete roles of multiple phosphorylation sites in the Fanconi Anaemia DNA repair pathway

P57 **Tsingos, Erika**
T22 *How tissues coordinate growth in an organ: Insights from modeling clonal lineages in fish*

P58 **Tuckwell, Andrew**
T17 *An engineering approach to molecular assembly of the Type 3 Secretion System*

P59 **Volkova, Nadezda**
Mutational signatures of DNA repair deficiencies and cytotoxin exposures in C. elegans

P60 **Wandzik, Joanna**
Structural study of the catalytic domain of RNase E

P61 **Wang, Jiang-Hui**
Transforming Growth Factor beta-Activated Kinase 1 (TAK1) is a novel target for retinal neovascularisation

P62 **Wiegand, Tina**
Force measurements of single virus particle uptake

P63 **Yserentant, Klaus**
T8 *Towards quantitative 3D fluorescence microscopy with CoPS and array tomography*

Poster Abstracts

P1 Utilising the benefits of whole exome sequencing to advance efforts in Familial Hemiplegic Migraine diagnostics

Albury, Cassie; Maksemous, Neven; Smith, Robert; Haupt, Larisa; Griffiths, Lyn

Genomics Research Centre, Queensland University of Technology, Australia

Familial Hemiplegic Migraine (FHM) is an autosomal dominant neurological condition. Attacks are characterized by severe head pain, nausea, aura, phono/photophobia & hemiparesis. In rare instances, additional episodes of either/or - fever, seizures, prolonged weakness & coma can develop. For a small minority, residual symptoms of memory loss & attention deficits may continue for a few weeks to months. 20% of affected FHM individuals develop a mild but permanent form of ataxia & nystagmus which may worsen with time. FHM symptomology is vast & varied amongst the population & can often overlap with a number of similar neurological disorders - making it difficult to diagnose. Due to limitations in analytics, FHM diagnostic success rates are low (<20%), treatment is sub-par & the understanding behind the pathophysiological consequence of geno-phenotype association is constrained. We have applied Whole Exome Sequencing (WES) to a cohort (n=17) of clinically suspected & genetically undiagnosed FHM patients for the identification of new diagnostic markers. Using a developed bioinformatics modelling approach, we have begun data analysis by filtering variants based on gene ontology, associated pathways, MAF & various predicitive functional scores. Using this method of analysis we have identified a candidate mutation list to be validated & tracked through family lineages where possible. The genetic nature of FHM presents complications of polygenism and heterogeneity; hence, we expect to identify a number of different genes associated with its cause. Preliminary results have revealed some interesting candidate genes associated with vascular function & regulation, neurological homeostasis, ion channel function, metal trafficking & small indications of immune system & muscle stability association.

P2 Degradation of volatile hydrocarbons in estuarine environments

Amande, Tivkaa; McGenity, Terry

University of Essex, United Kingdom

There is a gap in our understanding of the anaerobic degradation of isoprene and the non-methane gases especially ethane. This project seeks to understand the fate of five volatile hydrocarbons, namely isoprene, ethane, propane, benzene and toluene, due to microbial degradation in estuarine environments. Degradation was investigated in aerobic and anaerobic sediment slurry microcosms with samples collected at three locations along the Colne estuary in Essex, UK. Hydrocarbon loss due to degradation was monitored using gas chromatography coupled with flame ionisation detection. Significant aerobic degradation of each hydrocarbon occurred. Anaerobic degradation of toluene and benzene was observed, while isoprene, ethane and propane degradation was not seen even after 150 days' incubation. In aerobic microcosms, more than 80% benzene and toluene degradation was observed within six days and ten days for isoprene degradation. Ethane and propane degradation was generally slower and only about 60% degradation was observed with both carbon sources after 57 days. Analysis of the bacterial 16S rRNA gene sequences and denaturing gradient gel electrophoresis indicated that the main aerobic benzene-degrading bacteria were *Pseudomonas* spp. and the main toluene-degrading bacteria were *Amphritea* spp., while the isoprene-degrading communities were dominated by *Rhodococcus* spp. The ethane- and propane-degrading communities were a mixture of Alpha-, Beta- and Gamma-proteobacteria. Understanding the role of aerobic and anaerobic volatile hydrocarbon-degrading microbial communities will increase our knowledge of how these compounds are cycled in the marine environment.

P3 Group Factor Analysis to disentangle common and specific sources of variation between different biological layers

Argelaguet, Ricard; Stegle, Oliver; Buettner, Florian

EMBL-EBI Cambridge, Spain

Factor Analysis is a cornerstone of classical data analysis. It decomposes a multivariate dataset of correlated variables in terms of a potentially smaller number of uncorrelated variables. However, the method is not appropriate to sistematically analyse data sets consisting of multiple input matrices (views) of co-occuring samples.In this master thesis we developed single-cell Group Factor Analysis (scGFA), a fully bayesian latent variable model with an accurate noise and likelihood assumptions which is able to integrate information from different biological layers. scGFA is a multi-view extension of factor analysis that disentangles the variation unique to a single view and the variation shared between multiple views. We applied the scGFA model to a data set of 61 Embryonic Stem Cells generated by a technology called scMT-seq, a recent method that performs a parallel profiling of the DNA methylation and the gene expression in single cells. Our results show the existence of several independent axis of variation and allowed us to identify three clear subpopulations that are associated with different pluripotency potential and genome-wide methylation rate.

P4 Long-read sequencing analysis of the dynamic transcriptome of the *Pseudorabies* virus

Balázs, Zsolt; Tombácz, Dóra; Csabai, Zsolt; Moldován, Norbert; Sharon, Donald; Snyder, Michael; Boldogkoi, Zsolt

University of Szeged, Hungary

Long-read sequencing is a powerful tool in identifying novel transcripts and transcript isoforms. Our group has previously utilized long-read sequencing methods for annotating numerous novel transcript isoforms in the *Pseudorabies* virus (PRV) transcriptome. In this study we present the quantitative analysis of the dynamic transcriptome of this herpesvirus using long-read sequencing data. PolyA-selected RNA was isolated from PRV-infected PK-15 cells 1h, 2h, 4h, 6h, 8h and 12h after infection. The isolated RNA was reverse transcribed to double-stranded cDNA which was then sequenced by Pacific Biosciences Single Molecule, Real-Time sequencing platform following the Very Low (10 ng) Input 2 kb Template Preparation and Sequencing with Carrier DNA protocol. Reads were mapped to the PRV genome using GMAP. The 6 samples of different post infection times yielded altogether 54,467 viral reads with a mean read length of 1,287 nucleotides and the majority of the PRV transcript isoforms was represented by at least one read in each sample. The kinetics of the PRV transcripts were characterized by the changes in the relative amounts of reads aligning to them in the different samples. We also normalized our read counts to the number of reads aligning to the swine (*Sus scrofa*) mitochondrial genome to show the overall increase in the relative number of viral reads in the later stages of infection. Normalization by the changes of the relative amounts of viral DNA in our samples showed a drastic drop of the viral gene expression per genome after 4h post infection. Our results are mostly concordant with previous kinetic characterizations of PRV transcripts using RT-qPCR with the distinction that RT-qPCR analysis cannot differentiate between transcript isoforms, while long-read sequencing can. Our study shows that long-read sequencing data is an effective tool for quantitative analysis of transcripts.

P5 Crystallization of the inner membrane protein SbmA from *Escherichia coli*

Bartels, Kim

EMBL Hamburg, Germany

SbmA is an inner membrane protein from *Escherichia coli*. It is a dimeric transporter which has been shown to import a variety of substrates like the antibiotic bleomycin as well as microcins, proline-rich antimicrobial peptides and peptide nucleic acids, which are harmful to the cell, into the bacterial cytoplasm. Whilst the physiological function and the structure of SbmA are not known, it is sometimes suggested that SbmA is a member of the ATP-binding cassette transporter superfamily. It displays homology to the transmembrane domain of ATP-binding cassette transporter but it does not possess a nucleotide binding domain and utilizes an electrochemical gradient rather than ATP hydrolysis to transport its substrates across the membrane. In this work SbmA crystals were grown to obtain good resolution data. For this purpose SbmA in different detergent micelles or mixed detergent micelles was crystallized. SbmA was also co-crystallized with crystallization chaperones like antibody fragments or nanobodies. In addition SbmA was crystallized in lipid cubic phase. Crystals were successfully grown for SbmA in mixed detergent micelles and in lipid cubic phase but these crystals have not been tested yet for their diffraction properties. Crystals were obtained for SbmA crystallized with antibody fragments as well. These crystals diffracted to a maximum resolution of 5.5 Å. Taken together this work provides newly identified crystallization conditions for SbmA using the vapor diffusion method as well as in lipid cubic phase. Upon optimization these conditions could be used for structure determination of SbmA.

P6 Reverse Engineering EMT

Becker, Kolja; Garding, Angela; Sahu, Sanjeeb; Schick, Sandra; Patil, Shankarrao; Tiwari, Vijay; Legewie, Stefan

Institute of Molecular Biology Mainz, Germany

Epithelial-to-Mesenchymal Transition (EMT) is a reversible trans-differentiation event by which epithelial cells loose some of their defining characteristics and gradually switch to a more motile and invasive mesenchymal phenotype. Hallmark of EMT is the down-regulation of certain cell adhesion factors such as E-Cadherin, accompanied by an up-regulation of N-Cadherin. EMT is involved in many biological processes such as organogenesis and wound healing, but is also known to associate with cancer metastasis.In the process of EMT many cell and tissue characteristics are affected, such as changes in cell morphology, cell size and cell polarity, disintegration of cellular junctions and arrangement of the extracellular matrix. These phenotypical changes need to be adequately coordinated. In NMuMG cells EMT can be induced by stimulation of cells with TGF-ß, which is followed by an activation of the SMAD-signaling pathway. The further progression of EMT is then tightly controlled by a gene regulatory network composed of a number of transcription factors and downstream effector genes. However, this gene regulatory network remains incompletely characterized. From an extensive literature research, a number of putative transcription factors involved in EMT was selected for knock-down. These transcriptions factors as well as further effector genes, controlling the phenotypic changes during EMT, were subsequently measured at various time-points after TGF-ß stimulation. The experimental data served as an input into different state-of-the-art network inference tools. Individual results of the network inference tools were integrated into a community prediction, which could then be used as a basis to fit a dynamical model to the time-course and knock-down data. Such a dynamical model will aid our understanding of the process of epithelial-to-mesenchymal transition in health and disease and might even trigger the development of new therapies against the progression of tumors via EMT.

P7 Quantitative structural information from single molecule FRET

Beckers, Maximilian; Eilert, Tobias; Drechsler, Florian; Michaelis, Jens

EMBL Heidelberg, Germany

Single-molecule studies can be used to study biological processes directly and in real-time. In particular, the fluorescence energy transfer between reporter dye molecules attached to specific sites on macromolecular complexes can be used to infer distance information. When several measurements are combined, the information can be used to determine the position and conformation of certain domains with respect to the complex. However, data analysis schemes that include all experimental uncertainties are highly complex, and the outcome depends on assumptions about the state of the dye molecules. Here, we present a new analysis algorithm using Bayesian parameter estimation based on Markov Chain Monte Carlo sampling and parallel tempering termed Fast-NPS that can analyse large smFRET networks in a relatively short time and yields the position of the dye molecules together with their respective uncertainties. Moreover, we show what effects different assumptions about the dye molecules have on the outcome. We discuss the possibilities and pitfalls in structure determination based on smFRET using experimental data for an archaeal transcription pre-initiation complex, whose architecture has recently been unravelled by smFRET measurements.

P8 Origin, functional diversification and substrate specificity determinants in the family of NCS1/FUR transporters

Bobonis, Jacob; Krypotou, Emilia; Pittis, Alexandros; Evangelidis, Thomas; Gabaldón, Toni; Scazzocchio, Claudio; Mikros, Emmanuel; Diallinas, George

EMBL Heidelberg, Germany

Functionally characterised NCS1 (Nucleobase Cation Symport 1) proteins in bacteria, fungi and plants are substrate:proton symporters, specific for the salvage of purines, pyrimidines and related metabolites, such as vitamins and drugs. NCS1 proteins possess 12 a-helical TransMembrane Segments (TMS), 10 of which are arranged in two inverted repeats of 5 helices. We present a phylogenetic analysis of NCS1 proteins, suggesting their independent origin through horizontal gene transfer from prokaryotes, and expansion by gene duplication of the two fungal NCS1 subfamilies (Fur and Fcy). Plant NCS1 are also shown to originate from prokaryotes, whereas NCS1 proteins are absent in protozoa and metazoa. To understand the evolution of the functional diversity of the NCS1 proteins, we characterized all 7 NCS1/Fur proteins, of the model fungus *Aspergillus nidulans*, uncovering previously unknown functions and specificities. To understand the molecular details that distinguish members of the Fur subfamily, we performed homology modelling, substrate docking and molecular dynamics (MD) in three major Fur transporters, with distinct specificities (FurD: uracil; FurA: allantoin, FurE: uric acid, uracil, allantoin). We identify residues critical for substrate binding, transport and specificity, in TMS1, TMS3, TMS6 and TMS8 and confirm their functional importance through a systematic mutational analysis. We predict and confirm that substrate specificity determinants are located not only in the major substrate-binding site (TMS1, TMS3, TMS6 and TMS8), but also in a putative outward-facing gate (TMS10). This result supports emerging evidence for the presence of channel-like gates in transporters and extends their role in substrate selection.

P9 Interactions between astrocytes and synapses in a rat animal model of epilepsy

Boissonnet, Tom; Pernet Gallay, Karin; Fertin, Arnold; Jouneau, Pierre-Henry; Guillemain, Isabelle; Usson, Yves

EMBL Monterotondo, Italy

Epilepsy is a neurological disorder characterized by recurrent spontaneous seizures due to hyperexcitability of neurons. Our preliminary data indicate a significant contribution of astrocytes in the pathophysiology of epilepsy. Therefore, interactions between astrocytes and synapses in a rat model of epilepsy (GAERS) has been investigated at the ultrastructural level.For this, 3D electron microscopy was implemented by using a Focused Ion Beam/Scanning Electron Microscope (FIB/SEM) to image volumes of more than 1000 µm3 at 4 nm resolution in all directions within the cortical region generating seizures before and after the onset of epilepsy. Since the information available within the stacks obtained by FIB/SEM is of a high complexity, 3D segmentation has been done with ilastik software to isolate synapses and astrocyte allowing a full 3D reconstruction so that the percentage of synaptic covering by astrocytes could be measured. To facilitate the alignment and the preparation of the stack, several macros have been written for imageJ. It was however difficult to handle our image stacks with our computer resource, therefore each stack were split in four, and the mesh of the cleaved segmented objects were sewn with a plugin written for this purpose.

P10 SMC4 is essential for sporozoite formation in the Malaria parasite

Boucher, Matthew

EMBL Heidelberg, United Kingdom

Malaria is a prevalent disease in the developing world, and is caused by the unicellular apicomplexan parasite, *Plasmodium*. *Plasmodium* undergoes atypical mitotic and meiotic divisions and it is not well known how they are controlled and regulated. This project used the murine parasite, *Plasmodium berghei* to report on the expression and function of Structural Maintenance of Chromosomes 4 (SMC4) in parasite cell division. SMC4 is a member of the SMC family of proteins, which are highly conserved and important for chromosome dynamics in eukaryotes and prokaryotes. SMC4 typically forms part of the condensin complex, which has functions including facilitating chromosome condensation – a process that does not happen in *Plasmodium* cell division. Three genetic constructs were produced to assess expression and function of SMC4: SMC4 expressed under the control of the ama1 promoter, SMC4 tagged with GFP (fluorescing green) and SMC4 tagged with mCherry (fluorescing red). Putting SMC4 under the control of the ama1 promoter allowed it to be expressed only in blood stages, allowing knock-out assessment of the other stages without compromising life cycle progression (SMC4 was previously determined to possibly be essential at the blood stage). SMC4-GFP and SMC4 promoter-swap transgenic parasites were produced, but SMC4-mCherry failed to be transfected. We observed that SMC4 was primarily expressed in the nucleus in the life cycle stages studied and that SMC4 was important for exflagellation of male gametocytes, zygote to oocyst transition, oocyst development and was essential for sporozoite development in oocysts. SMC4 knock-out parasites produced small oocysts which failed to produce sporozoites. Future work could elucidate the precise function of SMC4 in the malaria parasite. A greater understanding of the functions of SMC4 and other molecular players in *Plasmodium* cell division could allow for the identification of drug targets that inhibit malaria life cycle progression.

P11 Age-dependent changes in the expressed immunoglobulin repertoire of a short-lived teleost

Bradshaw, William; Valenzano, Dario Riccardo

Max Planck Institute for Biology of Ageing, Germany

Ageing individuals exhibit a pervasive decline in B-cell function, including decreased naïve B-cell production [1] and reduced antibody affinity [2]. These changes contribute to an overall immunosenescent phenotype, with important implications for health and lifespan. The diversity of the antibody repertoire is also widely thought to decrease with age [3]; however, the relatively long lifespan of most vertebrate model organisms has prevented a thorough investigation of this phenomenon. The recent development of the naturally shortlived killifish *Nothobranchius furzeri* [4] provides an exciting opportunity to investigate agerelated changes to the antibody repertoire in much greater detail than previously possible. Using high-throughput sequencing of longinsert clones from the killifish genome BAC library, I have sequenced and assembled the killifish immunoglobulin heavy chain locus to a high degree of accuracy and characterised the antibody gene segments it contains. Next, I will use the assembled locus to investigate the effect of ageing on the adaptive immune system in this model organism, by comparing the expressed antibody repertoires [5] of young and old fish cohorts. Additionally, I will characterise changes in expressed antibody repertoires following lifespanenhancing manipulations, such as dietary restriction [6] and gut microbial transfer. Further experiments will investigate strategies to improve killifish lifespan by targeting humoral immunity. The results of these experiments could have important implications for the broader understanding of humoral immunosenescence in clinical and other applied contexts.

[1] Weiskopf et al. (2009) Transpl. Int. 22(11):1041-1050

[2] Marshall-Clarke & H. Playfair (1975). Immunology 29(3), 477.

[3] Gibson et al. (2009) Aging Cell 8(1):1825.

[4] Harel et al. (2015) Cell 160(5):10131026.

[5] Georgiou et al. (2014) Nature Biotechnol. 32(2):158168.[6] Terzibasi et al. (2009) Aging Cell, 8(2):8899.

P12 A slimy situation: Using ‘omics and computational tools to understand the biochemical and biophysical properties of *Sepiadariid* slime.

Caruana, Nikeisha; Cooke, Ira; Faou, Pierre; Finn, Julian; Hall, Nathan; Norman, Mark; Pineda, Sandy; Strugnell, Jan

La Trobe University, Australia

Cephalopods comprise over 800 species, possess advanced nervous, cardiovascular and visual systems and are masters of camouflage. *Sepiadariidae*, one family of benthic squids, possess specialized systems of secretion, secreting a viscous slime from their underside. It is believed that these secretions are involved in defending the species from predators. These systems exhibit unique biochemical and biophysical properties such as dramatic volume expansion, adhesion and toxicity. Our project highlights a unique secretion mechanism in cephalopods in two particular squids within this family, *Sepiadarium austrinum* and *Sepioloidea lineolata*. Our study sheds light on this remarkable defence mechanism, using a combination of *de novo* assembled transcriptomes from various tissues (including the slime itself) along with proteomic analysis. These methods were complemented with bioinformatics analysis, incorporating the use of transcriptome annotation and phylogenetic analysis. In doing so we were able to identify likely functions for proteins within the slime. Within both species, a number of putative toxic proteins have been identified, along with proteins involved in the anti-microbial and immune response of the organism. Proteins within the slime have also been compared to the protein composition of hagfish slimes. Our work highlights potential similarities in the mechanism of the hagfish, with proteins involved in calcium regulation and intermediate filaments found abundantly in both species. In both *Sepiadariidae* squids no mucin protein, normally found in mucus secretions, were found within the slime. This indicates that the composition of the slime secretion occurs by a currently unknown mechanism. By identifying the proteins involved in the secretion, and the location and expression of these proteins within the species, we can start to uncover the mechanisms and biophysical properties of slime within these species.

P13 Whole genome view of the consequences of a population bottleneck using 2926 genome sequences from Finland and United Kingdom

Chheda, Himanshu; Palta, Priit; Pirinen, Matti; McCarthy, Shane; Walter, Klaudia; Koskinen, Seppo; Salomma, Veikko; Daly, Mark; Durbin, Richard; Palotie, Aarno; Aittokallio, Tero; Ripatti, Samuli

University of Helsinki, Finland

Isolated populations with enrichment of variants due to recent population bottlenecks provide a powerful resource for identifying disease-associated genetic variants and genes. As a model of an isolate population, we sequenced the genomes of 1463 Finnish individuals as part of the Sequencing Initiative Suomi (SISu) Project. We compared the genomic profiles of the 1463 Finns to a sample of 1463 British individuals that were sequenced in parallel as part of the UK10K Project. Whereas there were no major differences in the allele frequency of common variants, a significant depletion of variants in the rare frequency spectrum was observed in Finns when comparing the two populations. On the other hand, we observed >2.1 million variants that were twice as frequent among Finns compared to Britons and 800,000 variants that were more than 10 times more frequent in Finns. Furthermore, in Finns we observed a relative proportional enrichment of variants in the minor allele frequency range between 2 - 5% ($p < 2.2x10\text{-}16$). When stratified by their functional annotations, loss-of-function (LoF) variants showed the highest proportional enrichment in Finns ($p = 0.0291$). In the non-coding part of the genome, variants in conserved regions ($p = 0.002$) and promoters ($p = 0.01$) were also significantly enriched in the Finnish samples. These functional categories represent the highest a priori power for downstream association studies of disease associated rare variants using population isolates.

P14 Investigating the folding and insertion of bacterial outer membrane proteins by atomic force microscopy

Crosskey, Tom

EMBL Hamburg, Germany

The BAM complex is an essential heteropentamer composed of a central transmembrane component BamA and lipoproteins BamB-BamE, located in the outer membrane of all Gram-negative bacteria. It is responsible for folding and inserting outer membrane proteins (OMPs) using a mechanism not fully understood. In my MSc, I expressed and purified this complex as well as truncated versions of its components before carrying out biochemical and biophysical experiments in an attempt to elucidate this process further. These experiments included demonstrating binding interactions between the periplasmic domains (POTRA) of the main pore-forming component of the BAM complex (BamA) and unfolded OMPs, as well as between POTRA and OMPs in complex with periplasmic chaperones. I also demonstrated fluorometrically that the folding of OMPs by the BAM complex was dependent on the periplasmic chaperone SurA. Because protein folding *in vivo* is a physical event, I also used the atomic force microscope (AFM) to characterise the unfolding forces of the POTRA domains in an attempt to investigate the purpose of these domains and the role they play in OMP formation. I also measured the interactions between POTRA and OMPs using force spectroscopy on the AFM with and without the presence of chaperones to reveal more information about the way these vital proteins interact. The goal of this work was to unravel the mechanism of this complex and its associated proteins so as to provide a novel target for future research which would struggle to build up antibiotic resistance.

P15 A semi *in vivo* system for PML body research

Czuchnowski, Jakub; Rosen, Michael

EMBL Heidelberg, Poland

Recent studies show the rising importance of the intermediate scale of cell biology, spanning between protein complexes and classic organelles, this intermediate scale is inhabited by very large molecular structures called sometimes cellular puncta or membrane-less organelles. Understanding these objects would provide another big step in understanding life. Promyelocytic leukemia nuclear bodies (PML NBs) are a promising model for these structures, as they have only one identified component that is both required and sufficient for their formation, namely the PML protein. Difficulties with studying PML NBs stem from the inability to isolate them from cells in a unaltered state, that would preserve the natural protein composition of these structures. A nuclei isolation protocol was established, that would preserve the presence of PML NB in a semi-*in vivo* system, as a first step in the attempt to purify PML bodies with preserved composition.

P17 Ageing-related changes include increase in interaction entropy

Dönertas, Handan Melike; Isildak, Ulas; Izgi, Hamit; Somel, Mehmet

Middle East Technical University, Turkey

Ageing is associated with progressive decline in a variety of biological processes causing functional decline and loss of physiological integrity. However, the underlying mechanisms are still to be uncovered mainly due to heterogeneous and stochastic nature of ageing. In this study, we employ a meta-analysis scheme integrating protein-protein interaction and gene expression data to analyse ageing-related stochastic changes. Specifically, we use Shannon entropy to measure interaction promiscuity, and study how promiscuity varies among genes depending on network centrality and individual age. Preliminary analysis on brain ageing shows that genes that become more central in the PPI network with ageing also become more promiscuous. This raises the possibility that ageing-related gene expression changes may involve unspecific interactions and contribute to dysfunction. We will next analyse interaction entropy in other tissues and study the functionality of this system-level behaviour, to gain better understanding into its relevance to ageing and ageing-related diseases.

P18 Granulomatosis with Polyangiitis: Knowledge integration and network analysis towards mechanistic understanding of underlying pathogenesis

Duenas, Corina; Kronbichler, Andreas; Jayne, David; Hermjakob, Henning; Chelliah, Vijayalakshmi

EMBL-EBI Cambridge, United Kingdom

Granulomatosis with polyangiitis (GPA) (1) is a rare multisystem autoimmune disease targeting the respiratory tract, liver and kidneys. Its characteristic features include necrotizing granulomatous inflammation and pauci-immune vasculitis in small- and medium-sized blood vessels. The mechanism underlying the pathogenesis of GPA remains unknown although a number of exogenous factors, and genetic and protein biomarkers have been suggested to be of aetiological relevance. This makes the treatment less efficient and to date there is no complete cure for GPA. Here, we will explain how network-based analyses of omics data, in combination with functional and clinical studies, are aiding our understanding of the disease. We have compiled and integrated heterogeneous knowledge from several resources that includes meta-analysis (2), database resources and text-mining, and have generated a systems level mechanistic overview of GPA. These integrated multi-omics networks form a base for identifying the regulatory clusters that help to prioritize diagnostic markers or therapeutic candidate genes. We envision to build mathematical models describing the mechanism of key molecular targets of GPA derived from the above mentioned integrated knowledge network. This would allow us to provide mechanistic insights to different aspects of the disease, for example, immunological aspects of disease relapse, and resistance mechanism to a particular drug. We believe our analysis would help designing new therapies and clinical investigations for treating GPA.

1. Csernok E, Gross WL. Current understanding of the pathogenesis of granulomatosis with polyangiitis (Wegener's). Expert Rev Clin Immunol. 2013;9(7):641-8.

2. Kronbichler A, Kerschbaum J, Grundlinger G, Leierer J, Mayer G, Rudnicki M. Evaluation and validation of biomarkers in granulomatosis with polyangiitis and microscopic polyangiitis. Nephrol Dial Transplant. 2016;31(6):930-6.

P19 Gel-free mass spectrometry to explore the thiol proteome of chronic diseases

Duong, Nguyet

The University of Western Australia, Australia

Oxidative stress, caused by excessive reactive oxygen species (ROS), is evident in many chronic diseases. However, there is limited mechanistic information on how oxidation of multiple proteins is causing cell and tissue dysfunction. A systems biology approach has the potential to provide novel insights into mechanisms of action. I have focused on protein thiol oxidation because thiol groups (-SH) on cysteine residues of proteins are particularly sensitive to oxidation. As a consequence, changes in the function of multiple proteins caused by thiol oxidation has many aspects of cell and tissue function. In preliminary work using gel electrophoresis and mass spectrometry identification, I established that multiple proteins were undergoing thiol oxidation in muscles of a dog model for dystrophy. My project objective is to greatly increase the number of protein that can be identified in complex biological samples. I plan to do this by developing high throughput proteomic techniques using gel-free mass spectrometry. This approach will also generate information about the site of oxidation on proteins and the degree of oxidation. With this information, information about protein location, and involvement in molecular networks, I aim to identify molecular pathways that contribute to cellular dysfunction in diseases where oxidative stress is evident (e.g. muscular dystrophy).

P21 Membrane-mediated interaction of curvature-active proteins

Golushko, Ivan; Lorman, Vladimir; Rochal, Sergei

Université de Montpellier, France

We contribute to the study of intracellular and intercellular processes involving strong curvature variation of the cell membrane. We propose a model of the interaction between the adsorbed curvature-active proteins mediated by the lipid membrane strain field and apply it to the inter-protein interactions on the surface of a tubular lipid membrane (TLM). In the present work we focus on the anisotropy of the protein-tubule interaction and its description in the frame of the coarse-grain lipid bilayer elasticity theory. We model the action of curvature-active proteins with the help of the superposition of the delta-like point “forces” applied to TLM. The forces are localized in the area corresponding to the adsorbed protein and satisfy the mechanical equilibrium conditions. The developed multipole approach accounts for the interaction anisotropy and enables us to model the membrane-mediated interactions between the adsorbed finite-size anisotropic proteins. It opens the possibility to study the interactions of curvature-active proteins on surfaces with more complex biologically relevant geometries.Another important aspect of the present work is the analysis of the boundary conditions influence on the behavior of the model. Along with the conventional periodic boundary conditions we have examined the behavior of the TLM with pinned ends. We show that two specific regions emerge at the ends of the pinned TLM. In these regions the adsorption of proteins is much more energetically favorable than elsewhere on the TLM surface. This result is in a good agreement with the recent data obtained in a number of experiments on the adsorption of curvature-inducing proteins on TLMs. The results are illustrated on the examples of proteins possessing both BAR-domains and amphipathic helices, like endophilin

P22 A new drug discovery platform based on Bioluminescence Resonance Energy Transfer: bacterial interaction ß'-s70 interfering compounds identification

Guerra, Matteo; Sartini, Sara; Levati, Elisabetta; Montanini, Barbara

Parma University, Italy

Every cellular process, from cell cycle regulation to mRNA translation, involves protein-protein interactions. Their precise control suggests us new therapeutic approaches, being allies against the slowing down of the drug discovery process and helping us in facing new challenges, as antibiotic resistances. The BRET technology exploits the Resonance Energy Transfer, which happens between a light-emitting donor enzyme, and an energy acceptor protein, that emits fluorescence in response to the energy provided by the donor enzyme. Therefore, the dynamics of protein-protein interaction can be studied *in vivo* by expression of chimeric protein pairs bearing the donor/acceptor moieties fused to two specific interaction partners: so that a BRET signal can be measured only if the two partners interact. The ultimate goal, once an interaction has been properly reconstituted and validated, is to exploit this technique to search candidate compounds capable of sharply decreasing the BRET signal.In this work we focused on the bacterial interaction ß'-s70, involved in transcription initiaition. All the possible construct combinations (e.g. switching between N- and C- terminal donor/acceptor's fusion) were created, to select the one that produces the best BRET signal. Afterwards, some specificity checks are essential: we tested the signal fall in the case of mutated interactors we have created, as well as the reliability of the signal by saturation curves.In order to validate the assay for Drug Discovery purposes, we recreated the s70 coiled coil structure, known to be essential for the s-ß' interaction, on a Thioredoxin scaffold, and used it as inhibitor surrogate.Furthermore, we expressed and purified the before-mentioned bacterial subunits (tagged) to set up an ELISA screening with the aim of confirming the inhibition observed in the BRET screening and make the two signals comparable. Finally, we screened a library of 5000 molecules, to find potentially antibacterial compounds.

P23 Theoretical models for nuclear pore complex assembly

Harsh, Moshir; Politi, Antonio; Otsuka, Shotaro; Padgett, Joe; Ellenberg, Jan

EMBL Heidelberg, Germany

The nuclear pore complex (NPC) is the largest non-polymeric protein complex in eukaryotic cells, which consists of over 500 proteins (nucleoporins) and mediates all transport between the nucleus and the cytoplasm. Upon entering mitosis, NPCs disassemble and at anaphase, the bulk of NPCs reassemble through a post-mitotic assembly pathway within a few minutes. A second assembly pathway during interphase is then required to insert new NPCs into the intact, growing nucleus to maintain a constant NPC density. Using non-equilibrium stochastic simulations we investigate the assembly kinetics, order and the driving force behind the formation of this multi-protein NPC. The simulations are compared to quantitative fluorescence microscopy data resolving single pore to bulk dynamics. The resulting model is then used to bridge the gap between single pore dynamics and bulk assembly, and relate the area and volume of nucleus with the nucleoporin accumulation and transport through NPCs. We also propose an approach to verify experimentally the potential cooperative nature of NPC assembly.

P24 How to phase genomic data with indels? A comparative study

Hassan, Shabbeer; Chheda, Himasnhu; Helkkula, Pyry; Nunez-Fontarnau, Javier; Häppölä, Paavo; Surakka, Ida; Palta, Priit; Palotie, Aarno; Ripatti, Samuli

Institute for Molecular Medicine (FIMM), Finland

The estimation of haplotypes (group of genes that are inherited together from a single parent) from SNP genotypes, is commonly referred to as 'phasing'. Determination of haplotype phase is an important methodological issue as we are in the era of large-scale sequencing. Many of its applications, such as imputing low-frequency variants and characterizing the relationship between genetic variation and disease susceptibility, are highly relevant to sequenced data. Haplotype phase can be generated through laboratory-based experimental methods, or it can be estimated using computational approaches. As experimental determination could be very expensive, computational phasing along with imputation for genotyped chip data is generally the preferred solution. However, a major shortcoming of currently available phasing software are their inability to handle short insertions/deletions (indels) and longer copy number variants (CNVs). As indels and CNVs have been found to play an important role in both Mendelian and complex diseases, phasing of such indels is an important feature. The aim of this work is to use and compare currently available phasing software (SHAPEIT2 and EAGLE2) by calculating various statistical metrics (switch error rates, haplotype accuracy & imputation concordance) to evaluate solutions (indel omission, indel trimming, native EAGLE2 indel handling) for this burgeoning computational problem in genomics. Results from the ongoing work indicate that phasing with EAGLE2 in combination with indel trimming yield comparable values of genotype concordance to SHAPEIT2 (~96%) but with added advantage of reducing computational time by one-third (for chromosome 20, 8.2 hrs vs 23.5 hrs). Also, to check whether phasing influences the imputation accuracy we would be comparing the above solutions in different imputation frameworks (BEAGLE4 and IMPUTE2).

P25 The Notch1 trimeric transcription factor complex regulates HEY1 in a cooperative manner

Hollmann, Nele; Mörtl, Fabian; Hennig, Sven

EMBL Heidelberg, Germany

Notch1 is a metazoan transmembrane receptor with a highly conserved signaling pathway, important during cell growth and proliferation. After ligand specific binding Notch1 is cleaved, releasing an intracellular domain, which translocates into the nucleus. Subsequent translocation and complexation with CSL (DNA binder) and MAML1 (stabilizer) leads to the transcriptionally active heterotrimer (NTC). During my studies I investigated a yet unknown arrangement of the NTC on the HEY1 promoter. NTCs bind to specific sequences within promoters. Up to now two distinct binding modes are known: (a) one NTC binds to a single binding site and (b) two NTCs bind to a double site with the complexes facing each other. However, the human HEY1 promoter includes two binding sites arranged "in row". I therefore investigated if the 2 complexes interact and if this interaction has any influence on the transcriptional activation.

P26 Analyzing growth and carboplatin sensitivity of ovarian cancer cells in 3D cell culture using confocal microscopy

Jann, Cosimo; Neugebauer, Julia; Zickgraf, Franziska; Sprick, Martin; Eils, Roland; Conrad, Christian

EMBL Heidelberg, Germany

Ovarian cancer has a worldwide incidence of more than a quarter million women annually. Due to its unspecific symptoms, it is mostly diagnosed in a late disease stage, when metastasis has already occurred. Current clinical therapies have only poor chances of success in these late cancer stages, raising the need of novel drugs and assays to test their efficiency in individual patients (personalized medicine). Within the scope of a 3-month research internship in the group of Dr. Christian Conrad at DKFZ [Intelligent Imaging], I analyzed phenotypic growth properties of two primary ovarian cancer cell lines in 3D cell culture, as well as their sensitivity to the chemotherapeutic agent carboplatin. Cells were seeded on a basal membrane-like matrix (matrigel), in which they form micro spheroids [Fig. 1 & 2]. Micro spheroids mimic tumor growth more accurately compared to conventional 2D cell culture, and also form during the course of ovarian cancer in the human abdomen. The spheroid cultures were imaged with a confocal laser scanning microscope over 15 days of growth, using fluorescent dyes and an endogenous H2B-GFP histone tag. An analysis workflow [steps illustrated in Fig. 3] generated with the software KNIME (University of Konstanz) allowed for the quantification of growth parameters, such as spheroid diameter, roundness and number of nuclei per spheroid [Fig. 4]. In addition, I established and used a microscopic assay to determine the LD50 (lethal dose 50) of carboplatin for the two cell lines in 3D culture [Fig. 5]. The carboplatin LD50 of the two cell lines (431 µM & 44 µM, respectively) are in a range comparable to other cancer cell lines growing in 3D culture, which are typically higher compared to 2D cultures. The established LD50 assay can be used to microscopically determine LD50 values of various drugs and drug combinations for other cell lines in spheroid culture, and can therefore contribute to the development of effective individual cancer therapies.

P27 Methods for simulating molecule diffusion for agent-based *in silico* models of biological systems

Jarrett, Simon; Timmis, Jon; Coles, Mark

University of York, United Kingdom

Diffusion is the movement of molecules from areas of high concentration to areas of low concentration. Cells such as T-cells depend on diffusion for their function: receptors on the cell surface that bind to specific cytokines and the cytokine secretion by the cell together allow for communication with other immune cells. Therefore, it is often necessary to also model diffusion when modelling cells *in silico*. Molecules are an order of magnitude smaller than cells, but their numbers are orders of magnitude greater. Simulating their individual behaviour thus quickly becomes infeasible. Typically, molecules are modelled *in silico* as concentrations on a discrete grid. Diffusion is then simulated by iterating through the grid and moving molecules to adjacent grid spaces (the neighbourhood), often using a discretised derivation of Fick's Law to dictate how fast molecules move between grid spaces. In agent-based models, a cell can then interact with the grid by secreting to and binding to molecules in nearby grid spaces. Abstraction of molecules and diffusion to a discrete grid makes the problem feasible, but it remains computationally expensive. Additionally, modelling diffusion in a discrete grid has other technical drawbacks and limiting factors that need to be addressed. These include: anisotropy, the tendency to diffuse faster along certain axes; the courant condition, a condition related to the maximum speed a molecule can move; and boundary conditions, which need to be carefully implemented to prevent artefacts occurring at the edges of the grid. Firstly, we analyse methods of simulating diffusion computationally, including the use of parallelism. Secondly, we analyse the effect changing the neighbourhood has on the computation time and accuracy of the diffusion, using the mean squared displacement as a measure. Lastly, we use a case study to determine whether the method of simulating diffusion affects the results of an agent-based *in silico* model of cell movement.

P28 Targeting Bax transmembrane domain oligomerisation

Juyoux, Pauline; Lucendo, Estefanía; Pardo, Nereida; Sancho, Mónica; Orzaez, Mar

EMBL Grenoble, France

The pro-apoptotic Bcl-2-associated X protein (Bax) has a central role in the mitochondrial outer membrane permeabilisation, which is a key step in the activation of the intrinsic apoptosis pathway [1-2]. Apoptosis over-activation has been co-related with several diseases, such as neurodegenerative disorders, cardiovascular diseases, or ischemia-reperfusion associated pathologies [3–5]. A detailed understanding of the Bax molecular mechanism of action may help in finding new points of pharmacological intervention to modulate their activity under pathological situations. Bax resides in the cytosol and translocates to the mitochondrial membrane upon activation by a cell death stimulus. This produces conformational changes of the protein that lead to the insertion, oligomerisation and pore formation in the mitochondrial membrane, releasing to cytosol pro-apoptotic molecules such as cytochrome c [6]. Recent studies suggest the relevant role of Bax transmembrane domain (Bax-TMD) in the modulation of apoptosis [7]. Using a bacterial system to monitor oligomer formation, we have performed a drug screening assay and identified FDA-approved drugs capable of inhibiting the Bax-TMD homo-oligomerisation. Studies on cell cultures demonstrated the ability of two of these compounds to protect human cells from death induced by the BH3 mimetic molecule ABT-263. These re-purposed Bax inhibitors would be useful tools to validate Bax-TMD surface of interaction as a new target for disease treatment.

1. Czabotar, P. E. Nat. Rev. Mol. Cell Biol.15, 49–63 (2014).
2. Youle, R. J. & Strasser, A. Nat. Rev. Mol. Cell Biol.9, 47–59 (2008).
3. Fuchs, Y. & Steller, H. Cell147, 742–58 (2014).
4. Cavallucci, V. & D'Amelio, M. Curr. Pharm. Des.17, 215–29 (2011).
5. Madathil, R. J. et al. Resuscitation105, 85–91 (2016).
6. Subburaj, Y. et al. Nat. Commun.6, 8042 (2015). 7. Zhang, Z. et al. EMBO J.35, 208–236 (2015).

P29 Conformational sampling using genetic algorithm and its comparative analysis with respect to systematic search

Kantamneni, Sravya M.; Sastry, Madhavi; Gottipati, Ragini; Sachchidanand, Sachichidanand; Tamzin, Victor

EMBL Hamburg, Germany

The success of the docking programs depends on the appropriate sampling of conformers and accuracy of the scoring function. To ensure a good start, it is always important to have a meaningful set of conformers which have a good probability of reproducing experimental binding pose. The challenging task in developing a sampling algorithm in spite of finding global minima without getting entrapped in local minima's, is to maintain the balance between the coverage and the exhaustiveness of the sampling procedure.Our study aimed at developing a small molecule conformational search tool using genetic algorithm which can address the problems in conformational search step of docking protocol with emphasis on providing a set of "pre-generated" conformers. Further, a comparative study was performed against systematic search to estimate the performance of the algorithm on selected test case. The study showed promising results with RMSD of docked pose less than 2Å in comparison with the experimental binding pose. Its further applicability can be established by testing on significant amount of the data.

P30 Deep mutagenesis and functional analysis of the pilin protein from *Neisseria meningitidis*

Kennouche, Paul; Duménil, Guillaume

Institut Pasteur, France

Neisseria meningitidis is an obligate human pathogen. It is one of the causative agents of meningitis and sepsis. In order to trigger pathogenesis, *N. meningitidis* depends on the expression of Type IV Pili (T4P) [1]. These micrometer-long appendages mediate several functions, including adhesion to eukaryotic cells, interbacterial aggregation and competence for transformation. While the expression, assembly and control of T4P are mediated by a complex machinery, the extracellular pilus fiber is a simple homopolymer of the pilin protein PilE. A recent body of evidence indicates that this protein could be the main mediator of T4P functions although the underlying mechanism is unknown [2,3]. Here, we conducted a high-throughput approach combining deep mutagenesis of pilE and functional analysis. Mutants from our library were selected for piliation as well as adhesion, competence and aggregation. The pilin sequences of the initial library and the positively selected mutants were then quantitatively compared using next-generation sequencing. Associated with structural modeling of the pilus fiber, this screen provides us with a quantitative functional mapping of the pilin protein at the amino acid resolution. We could identify specific areas involved in each T4P-mediated function. This work supports the idea that PilE is responsible for the different functions of T4P. It also suggests that the pilus fiber displays several distinct functional surfaces despite the small size of the pilin subunit.

[1] Melican Keira, et al. PLoS Pathog 9.1 (2013): e1003139.

[2] Imhaus Anne-Flore, and Guillaume Duménil. The EMBO journal (2014): e201488031.

[3] Miller Florence, et al. MBio 5.1 (2014): e01024-13.

P31 Development of a bioinformatics tool for *de novo* identification of microRNAs

Kentepozidou, Elissavet; Vitsios Dimitrios; Davis, Matthew; van Dongen, Stijn; Enright, Anton

EMBL-EBI Cambridge, United Kingdom

microRNAs (miRNAs) are small non-coding RNAs that play important roles in regu-lating gene expression in animals, plants and viruses. Their target genes are involved in a wide range of biological processes, from development and differentiation, to im-mune responses and cancer. Investigation of the biological roles of miRNAs requires that miRNA molecules have been identified and annotated. A number of specialised data-mining algorithms have been developed to facilitate the task of miRNA discov-ery in various species. However, none of these algorithms can aid miRNA detection without using a reference genome assembly. This sets an important limitation in investigating miRNA expression in species for which there is no reference genome available. To address this issue we developed miRnovo, a user-friendly bioinformat-ics tool capable of identifying miRNAs from small RNA-sequencing (sRNA-seq) data *de novo*, i.e. without using a reference genome. miRnovo groups sRNA-seq reads into clusters according to their sequence similarity and, subsequently, classifies the generated read clusters as miRNAs or non-miRNA transcripts using machine learn-ing methods. The performance of the miRnovo software was tested on a number of benchmark datasets from model organisms with well-studied and documented miRNA expression. miRNAs were identified by miRnovo with an accuracy of 80-90%, showing a good performance for the newly developed tool.

P32 Characterization of muscle regulator ANKRD1 in glioblastoma cell lines U87-MG and LN229

Kojic, Ana; Jasnic-Savovic, Jovana; Radojkovic, Dragica; Kojic, Snezana

EMBL Heidelberg, Germany

ANKRD1 protein is a member of the striated muscle specific MARP (muscle ankyrin repeat proteins) family. It functions as a mechanical stress sensor located in the I-band mechanosensory complex. ANKRD1 is predominantly expressed in cardiac muscle, but its expression is induced in skeletal muscle upon mechanical stress and in pathological conditions (spinal muscular atrophy, Duchene muscular dystrophy, amyotrophic lateral sclerosis). Mutations in ANKRD1 gene have been detected in patients with hypertrophic and dilated cardiomyopathies. Regarding cancers, it has been studied in ovarian tumor and rhabdomyosarcoma, but its role in molecular mechanisms of carcinogenesis is not well understood. It is interesting that ANKRD1 is functionally related to tumor suppressor p53. To study ANKRD1 in tumors we choose glioblastoma cell lines U87-MG and LN229. They express ANKRD1 at very low levels as determined by qRT-PCR and western blot analysis. ANKRD1 is predominantly localized in the nucleus, where both diffuse and spotted patterns were observed. Sequence analysis of ANKRD1 cDNA originating from both U87-MG and LN229 cells revealed several single point mutations. Three of them lead to amino acid substitutions. The use of anti-tumor drug doxorubicin is limited in glioblastoma treatment, because of difficult delivery. As well, it has cardio toxic effect. It is already demonstrated that doxorubicin inhibits ANKRD1 expression in cardiomyocytes. Interestingly, we have detected mild increase in expression of ANKRD1 in primary neonatal rat cardiomyocytes treated with doxorubicin, both on mRNA and protein levels. In conclusion, we preliminary characterized endogenous ANKRD1 in two glioblastoma cell lines and set the stage for future studies of ANKRD1 in tumor development and progression.

P33 A parametrized correlation measure model for enhancer-gene network inference in T cells

Kommer, Christoph; Zhang, Qin; Hegazy, Ahmed; Löhning, Max; Höfer, Thomas

German Cancer Research Center (DKFZ), Heidelberg, Germany

CD4+ T-helper cells direct the cell-based and antibody-based arms of the adaptive immune system via the secretion of cytokines. The classical view has been that naïve T-helper cells differentiate into a small number of distinct stable states that express certain cytokine profiles (Th1, Th2 etc.). Recently this view has been challenged by experimental findings that suggest a higher complexity: namely pointing towards a long-lived tunable continuum of cell states between the well-known extremes away from a bistable fixed-point solution. These hybrid states stably co-express graded levels of lineage-specifying transcription factors, such as T-bet and GATA-3. The mechanistic basis of such a stable continuum of cell states is unknown. To interrogate the underlying gene-regulatory mechanisms, we identified the enhancer landscape in naïve and differentiated T helper cells from histone modification patterns and found distinct classes of enhancers according to their regulation by lineage-specifying transcription factors and/or extrinsic differentiation signals. To this end, we developed a novel correlation model, via a parametrized multivariable histone correlation measure, for inferring enhancer-gene interactions on topologically associated domains. Using a combination of machine learning and bioinformatic algorithms we systematically identified enhancer states around relevant genes and mapped them to target genes; the mapping was refined using partial correlations. With this approach, we recovered well-known cis-regulatory elements and predicted new ones with comparable confidence. Using genetic perturbation of T-bet dose and different combinations of differentiation signals, as well as integrating information on enhancer activity with transcription factor binding data, allowed us to classify patterns of enhancer regulation. We discuss the utility of these data to learn enhancer-based regulatory network topologies.

P34 Dynamic modeling of tumor initiation and progression

Körber, Verena; Höfer, Thomas; Schlesner, Matthias; Barah, Pankaj; Radlwimmer, Bernhard

German Cancer Research Center (DKFZ), Heidelberg, Germany

Many tumors are heterogeneous tissues consisting of two or more subclonal populations. Reminiscent of speciation in evolution, a common conception suggests repetitive cycles of mutation, selection and clonal expansion to shape this cellular diversity. Yet, the driving forces underlying tumorigenesis are incompletely understood. We combine stochastic simulations with whole genome sequencing data of patient samples to identify the key events that uncouple tumors from homeostatic cell turnover. Specifically, we are interested in the factors that (1) control the promotion of a single, malignantly transformed cell into a premalignant population and (2) the progression from a premalignant state to heterogeneous cancer. To this end, we simulated the fates of transformed hematopoietic cells with a stochastic model of proliferation, death and differentiation and found that the chances for long-term survival of a quasi-neutrally mutated clone depend on its origin in the hematopoietic lineage. To understand how such a clone progresses into a heterogeneous tumor, we complemented our analysis with whole genome sequencing data of 19 pairs of primary and relapse glioblastomas. Defining subclones as genetically identical populations we inferred heterogeneity by fitting a multinomial model to the read count data on mutations and copy number variations. Assuming unidirectional, binary branching processes to shape the observed heterogeneity, our preliminary results indicate that relapse tumors evolve from small, non-dominant confounder populations of restricted mutational profiles in the primary tumor. Extension of our tumor model to additional, non-neutral mutations along with integration of new sequencing data will refine our analysis and help us to improve our understanding of the mechanisms that govern tumor initiation and progression.

P35 Ribonomics of abundant chloroplast RNA binding proteins

Lenzen, Benjamin; Ruwe, Hannes; Schmitz-Linneweber, Christian

Humboldt University of Berlin, Germany

Chloroplast gene expression depends on hundreds of nuclear-encoded DNA- and RNA-binding proteins (RBPs). Most of the hitherto analyzed RBPs are highly specific RNA adaptors and show little expression variation under the various conditions tested. These are unlikely to be global regulators of gene expression. By contrast, there is a family of chloroplast proteins named cpRNPs that are expressed in response to light, temperature, and developmental cues. Also, they are post-translationally modified in response to light, which changes their affinity to RNA. We identified the genome-wide RNA ligands of cpRNPs using ribonomics approaches and showed that they are required for the stability and processing of most chloroplast mRNAs. Two of the ten cpRNPs in *Arabidopsis* are particularly important under cold stress conditions and one other is essential for seedling development. Since cpRNPs are most closely related to nuclear (and not cyanobacterial) RRM proteins, we conclude that they evolved in eukaryotes to manipulate large sets of chloroplast RNAs under changing environmental conditions. Investigation of their quantitative effect on transcript pools in the chloroplast will help to elucidate the role of cpRNPs in the acclimation of land plants to varying environmental conditions by changing chloroplast gene expression. Quantitative genome-wide approaches will be employed to assess the individual transcript pools of each cpRNP under different conditions. We intend to combine these data with transcription and translation rates under respective conditions, to eventually infer a model of gene expression in the chloroplast on a system-level.

P36 Modelling lymphocyte proliferation on the single cell level based on data from time lapse fluorescence microscopy

Liu, Liyan; Kan, Andrey; Leckie, Christopher; D. Hodgkin, Philip

The University of Melbourne, Australia

Lymphocyte proliferation is a fundamental characteristic of the response to antigenic stimulation, and is an essential process to protect the host organism. In order to understand this process, time lapse fluorescence microscopy coupled with single cell tracking has been used to allow collection of individual cell fluorescence profiles as well as lineage relations between cells. Here we study B cell responses to CpG stimulation using FUCCI transgenic mice, and mathematical modelling of single cell fluorescence profiles over time. Time lapse imaging has an inherent problem that the process of image acquisition distorts original images (e.g., by introducing uneven illumination) and leads to inaccurate measurements of single-cell fluorescence levels. In order to obtain a correct interpretation of the true fluorescence time courses, we have proposed novel approaches to eliminate all acquisition effects. We then developed mathematical models for corrected individual cell fluorescence profiles, and finally searched for patterns prominent across a population of responding cells. Our results show that the proposed correction methods efficiently remove the bulk of acquisition effects. Next, using single-cell time course models allows us to automatically identify transitions in cell cycle stages, and ultimately quantify relations between cell cycle progression in different generations.

P37 Variation in core and accessory genome of *Escherichia coli* isolated from soil from riparian areas in New York State

Maistrenko, Oleksandr; Bergholz, Peter

EMBL Heidelberg, Germany

Escherichia coli is constantly deposited into extrahost environment with varying biotic and abiotic factors. We evaluated genome-wide variation that is associated with persistence in soil from forests and agricultural fields in isolates of *E. coli* from phylogroups D and B1. Genome libraries were prepared using NexTera XT library preparation kit (Illumina, San Diego, CA) and sequenced using an Illumina HiSeq 2500. We performed genome composition analysis using GET_HOMOLOGUES software. Variant calling in core genome was performed using cortex_var and the Genome Analysis ToolKit. We used random forest to identify genetic variants associated with habitat. Sizes of core and pan-genome in phylotype D and B were 2,003 genes and 18,430 and 2,761 and 13,374 of genes, respectively. In phylotype D, HipA-HipB toxin-antitoxin system and prophage genes were more prevalent in field soil habitat. Isolates from forest soil were more enriched with genes of flagellar synthesis proteins, components of type VI secretory system and MazEF toxin/antitoxin system. We identified one missense variant in pabB (aminodeoxychorismate synthase, subunit I) gene that was associated with agricultural field soil and two missense variants in genes yliC (putative oligopeptide transporter) and ypdF (aminopeptidase) were associated with forest soil.

P38 Pairwise biomarker combinations and predictive modelling for breast cancer intrinsic subtypes

Milioli, Heloisa; Riveros, Carlos; Vimieiro, Renato; Berretta, Regina; Moscato, Pablo

School of Environmental and Life Science, The University of Newcastle, Australia

Multi-gene signatures have been explored to assess the breast cancer prognosis and survival, and more recently to predict the disease intrinsic subtypes. Molecular variants have been incorporated into the PAM50 method to classify samples into a particular subtype. In this study, we tested the hypothesis that combined biomarkers provide reliable and stable sample assessments and also bring new insights for predictive modelling. For this purpose, we designed a novel systematic approach that relies on mathematical formulation, feature selection and data mining to identify pairwise probes (meta-features) with a minimum template, able to predict the intrinsic subtypes. First, we expanded the PAM50 signature (50) and all Illumina probes (48803) in the METABRIC cohort by computing the pairwise differences of the expression levels for all possible pairs, for each sample. This mathematical formulation was further combined with two well-established feature selection methods, the CM1 score and the (a,ß)-k-Feature set, and an ensemble learning technique. The selected meta-features embedded into 22 independent classifiers demonstrated extensive predictive power on labelling samples. Results showed an 'almost perfect agreement' between labels assigned by the majority of classifiers and the subtypes in the data set, for 12 PAM50 (Fleiss' kappa, $\kappa \approx 0.84$) and 13 Illumina ($\kappa \approx 0.89$) meta-features. The agreement between different sample labelling scrutinised by the Adjusted Rand Index was 0.90 and 0.93, respectively. Overall, the systematic approach revealed the utility of pairwise combinations to uncover variant expression levels across intrinsic subtypes. Furthermore, the feature selection strategy relies on fewer constructs than current methods, 12 (18 genes) and 13 (23 probes) meta-features, for predicting subtypes. Our model provides an opportunity for wide application in a variety of data types and supports advances in translational science and applied medicine.

P39 Investigating residue coevolution in proteins from a structural perspective

Morgunov, Alexey; Feher, Norbert; Gunnarsson, Alex; Babu, Madan

MRC Laboratory of Molecular Biology, United Kingdom

In recent years, there has been remarkable progress in the development of computational methods for detecting evolutionary couplings between residues in proteins from multiple sequence alignments (MSA) of protein families. These methods have been successfully applied in predicting three-dimensional structures from amino acid sequences, as well as in identifying functionally important residues. One of the key limitations that hinder wider applicability and higher accuracy of the so-called coevolutionary methods lies in the fact that covariation between residues is not only a function of structural and functional relationships between them – two related components that are hard to disentangle in their own right – but also of potential interactions with other proteins and ligands, of phylogeny, and of stochastic noise in the imperfect MSA. In order to begin teasing apart the contributions of various sources of coevolution to the observed signal, in the first instance we looked at the structural and interaction components. We performed a large-scale analysis of protein structure datasets, focusing on statistics that describe types, expected distributions and propensities for specific structural residue contacts, and contacts arising from interactions between proteins and ligands, as well as within protein complexes. This quantitative information was compared directly to the output of best performing coevolutionary methods, and the expected distributions were subsequently used as prior information to improve the performance of some of the methods in detecting important residue couplings based on previously published datasets.

P40 Utilising whole-transcriptome time-series data to unravel microRNA regulatory networks

Muskovic, Walter N.

Children's Cancer Institute Australia, Australia

Following their discovery in *C. elegans* in the early 90's, microRNAs have emerged as powerful regulators of gene expression in several important biological processes. Indeed, a large part of the human genome is now thought to be regulated by microRNAs, yet the design principles underlying this regulation are poorly understood. Focusing on microRNA dysregulation in the primary brain tumour glioblastoma, our research suggests microRNAs are extremely dynamic transcripts, and the key to unravelling their endogenous function will require high-resolution coding and non-coding gene expression time series data. Recognising the importance of microRNA dynamics, we have generated whole-transcriptome RNA-seq time series of synchronised human glioblastoma cells. Co-opting time series analysis techniques from ecology and physics, we demonstrate that the post-transcriptional regulatory landscape is replete with non-linear (non-separable) dynamics and so cannot be studied piecewise, as a decomposable sum of independent parts. These results hint at a unifying principle behind microRNA regulation, suggesting many mRNA transcripts are in fact 'intended' for degradation.

P41 Studies of NKp30 oligomerization and ligand binding

Pažický, Samuel; Kalousková, Barbora; Bláha, Jan; Vanek, Ondrej; Skálová, Tereza; Harlos, Karl; Charnavets, Tatsiana

EMBL Hamburg, Germany

Natural killer (NK) cells are immune cells with the ability to recognize and eliminate tumor cells and some virus infected cells. A slight balance between signals coming from inhibitory and activating receptors may lead to activation of the cytotoxic mechanisms and subsequent apoptosis of a target cell. NKp30 is an activation receptor of NK cells with one Ig-like extracellular domain, which is connected to the transmembrane part via short ”stalk” domain [1]. NKp30 creates dimer and oligomers and its dimer is visible in the crystal structure. Crystal structure of the complex has also been solved with proteins expressed in bacterial expression system [2]. However, it was found that glycosylation and oligomerization of NKp30 as well as the length of its short ”stalk” domain impact its affinity to ligands [3].We expressed the above mentioned proteins in HEK293S GnTI- cell line to yield proteins with homogenous and well defined glycosylation. The proteins were characterized by mass spectrometry and protein-protein interaction was measured by isothermal titatrion microcalorimetry. The NKp30 oligomers were also investigated by multiple methods, including analytical ultracentrifugation, aelectron microscopy, small angle X-ray scattering and glycosylated NKp30 was crystallized with B7-H6 as a complex. The results suggest that the NKp30 oligomerization is dependent on its glycosylation and that there is a dynamic equillibrium among various NKp30 oligomeric species.

[1] Vivier E. et al: Immunol Cell Biol, 92 (3), 221-9, 2014

[2] Joyce M.G. et al: Proc Natl Acad Sci U S A, 108 (15), 6223-8, 2011

[3] Herrmann J. et al: J Biol Chem, 289 (2), 765-77, 2014

P42 Metabolomics based pathway thermodynamics

Peña Navarro, David Alejandro; Gerstl, Matthias; Jungreuthmayer, Christian; Zanghellini, Jürgen

University of Natural Resources and Life Sciences, Austria

The laws of thermodynamics represent fundamental constraints for organisms. To derive these constraints the cellular metabolome is particularly useful as it determines the Gibbs energy surface, which allows us to draw conclusions on the directionality and feasibility of reactions and whole pathways. Thus we developed thermodynamic elementary flux mode analysis (tEFMA): a method that integrates the cellular metabolome into a metabolic pathway analysis and allows us to uniquely identify all thermodynamically feasible pathways. However, not all of these pathways can be combined into thermodynamically feasible flux distributions. In fact, we show that only a few out of all feasible pathways are biologically relevant and can be combined into thermodynamically feasible flux distributions. These pathways can be grouped into different sets of pathways, called largest, thermodynamically consistent (LTC) sets. We identify all of these LTC sets in *E. coli* and show that only a single LTC set is biologically relevant and is able to describe commonly available phenotypic data. This set is characterized by its ability to maximize biomass and ATP production, consistent with evolutionary interpretations of cell behavior. Moreover this LTC set unambiguously explains the experimentally observed behavior of glutamate dehydrogenase. In conclusion, we find that an LTC set fully determines all thermodynamically feasible capabilities of an organism and allows for a computationally efficient, unbiased, systems-level analysis of metabolism that delivers significant biological insight.

P43 *In silico* prediction of lncRNA function using tissue specific and evolutionary conserved expression

Perron, Umberto

EMBL-EBI Cambridge, Italy

In recent years long non coding RNAs (lncRNAs) have been the subject of increasing interest. Thanks to many recent functional studies, the existence of a large class of lncRNAs with potential regulatory functions is now widely accepted. Although an increasing number of lncRNAs is being characterized and shown to be involved in many biological processes, the functions of the vast majority lncRNA genes is still unknown. Therefore, computational methods able to take advantage of the increasing amount of publicly available data to predict lncRNA functions could be very useful. Since coding genes are much better annotated than lncRNAs, here we attempted to project known functional information regarding proteins onto non coding genes using the guilt-by-association principle. We computed gene coexpression for 30 human tissues and 9 vertebrates and mined the resulting networks with a methodology inspired by the rank product algorithm used to identify differentially expressed genes. Using different types of reference data we can predict putative new annotations for thousands of lncRNAs and proteins, ranging from cellular localization to relevance for disease and cancer. The data are available for download and through a user-friendly web interface at www.funcpred.com.

P44 Extending the simulation extrapolation (SIMEX) technique to pedigree reconstruction - a statistical method meets quantitative genetics

Ponzi, Erica; Muff, Stefanie; Keller, Lukas

University of Zurich, Switzerland

Pedigrees provide valuable information for quantitative geneticists, for instance to assess heritability, inbreeding, or inbreeding depression of phenotypic traits. Inbreeding depression is present when a fitness trait decreases due to an increase of inbreeding, i.e. when individuals have parents that are related to a higher degree. The effect can be quantified by regressing the trait on the inbreeding coefficient, where a negative slope indicates that inbreeding depression is present. Since the pedigree itself is often affected by error, due to misassigned paternities or missing information, the inbreeding coefficients are biased, and the inbreeding depression estimates are biased as well. Here we suggest a method to correct for these errors by generalizing the simulation extrapolation (SIMEX) idea to pedigrees. The SIMEX technique is an intuitive approach to correct for measurement error in regression models, where the idea is to add progressively more error, track the changes in the parameter estimates, and then extrapolate back to zero error. In a first phase, we simulate progressively increasing amounts of pedigree errors and plot the estimates of inbreeding depression as a function of the error proportion. In the second part we fit a function and extrapolate the value corresponding to zero error, estimating the correct level of inbreeding depression.We tested our approach on different types of pedigrees by varying the number of generations, total number of individuals and reproductive fraction of individuals per generation, and analyzed the effect of error in each case. We found a good agreement between the simulated real values of inbreeding depression and the error-free estimates we obtained from our algorithm. We are applying this method to real field data collected on a population of kestrels and on a population of song sparrows which show relevant amounts of missing (8%) and of misassigned (28%) paternities in the pedigree structures.

P45 The role of Evx in the locomotion of *Platynereis dumerilii* and its implication for Urbilateria

Puga, David E.; Martinez, Hernando; Arendt, Detlev; Richard, Freddie-Jeanne

EMBL Heidelberg, Germany

The locomotor system is well suited for evolutionary studies because its outputs are easy to measure and comparable across taxa. Previous studies have focused on describing these systems without providing an evolutionary framework to interpret this data. Furthermore, animal diversity is poorly represented, with most studies focusing on a few model species. The gene Evx is important for the specification of neurons of the locomotor systems of several model species. Its role has been described in representatives of the Ecdysozoan and Deuterostome taxa. But to infer whether this role was already present in Urbilateria, the last common ancestor of Protostomes and Deuterostomes, this description has to be extended to the Lophotrochozoan superphylum too. To address this problematic, we have studied the role of Evx in the locomotor system of *Platynereis dumerilii*, a model species that has risen for its suitability for evolutionary studies. We show that it is expressed exclusively in neurons and that knocking out this gene disrupts the locomotion of *Platynereis* larvae. We conclude that Evx specified neurons that were part of the locomotor system of Urbilateria.

P46 A kinetic model for chemical neurotransmission

Ramirez-Santiago, Guillermo; Martinez-Valencia, Alejandro; Fernandez de Miguel, Francisco

Universidad Nacional Autonoma de Mexico, Mexico

Recent experimental observations in presynaptic terminals at the neuromuscular junction indicate that there are stereotyped patterns of cooperativeness in the fusion of adjacent vesicles. That is, a vesicle in hemifusion process appears on the side of a fused vesicle and which is followed by another vesicle in a priming state while the next one is in a docking state. In this paper we present a kinetic model for this morphological pattern in which each vesicle state previous to the exocytosis is represented by a kinetic state. This chain states kinetic model can be analyzed by means of a Master equation whose solution is simulated with the stochastic Gillespie algorithm. With this approach we have reproduced the responses to the basal release in the absence of stimulation evoked by the electrical activity and the phenomena of facilitation and depression of neuromuscular synapses. This model offers new perspectives to understand the underlying phenomena in chemical neurotransmission based on molecular interactions that result in the cooperativity between vesicles during neurotransmitter release.

P47 Promiscuity of kinase superfamily as an effective platform for lead molecule screening

Ravikumar, Balaguru; Peddinti, Gopal; Tang, Jing; Parri, Elina; Timonen, Sanna; Wennerberg, Krister; Aittokallio, Tero

Finland Institute of Molecular Medicine, Finland

Protein sequence and structural similarities have been prominently used to estimate protein's relatedness in drug discovery applications. Recently, Similarity Ensemble Approach (SEA), a novel chemo-centric technique, was applied to estimate the similarity between protein targets by estimating the chemical similarity of the compounds that promiscuously bind to the given targets. SEA has been previously implemented and applied as a drug–repurposing methodology for the GPCR protein family. Protein kinases phosphorylate downstream proteins in signaling pathways and regulate various molecular processes, including the cell-cycle, differentiation, EMT and apoptosis. These pivotal roles in conjunction with their low- to mid-micromolar affinities to the co-factor ATP have made kinases as potential therapeutic targets in various carcinomas. With the aim to increase the number of putative small molecule kinase inhibitors, we have implemented a modified SEA as a novel *in silico* platform to screen and identify potent lead molecules targeting the kinase superfamily. The chemical similarity features were calculated from MACSS and ECF6 fingerprints, and the significance of the predictions were further refined through *in silico* docking studies. The GSK published kinase inhibitor set was initially used to evaluate the accuracy of the predictions of the *in silico* screening platform. Chemical diversity libraries from ChemBridge, ChemDiv, Tripos, Specs & Sigma, with approximately 130,000 compounds, were then used as the primary source of lead molecules. Through this platform, we have identified 36 potential compound-kinase interactions spanning across 25 possible lead molecules and 9 kinases belonging to various subfamilies, including ABL1, INSR, HCK, AKT1, AKT2, PRKAA2, EPHB4, PTK2 & MAPK7 kinases. Experimental validation of the model predictions is ongoing.

P48 Crystallization Screening of various Impß-H1-Imp7 constructs

Rojas Cordova, Carlos; Ivic, Nives

EMBL Heidelberg, Germany

The nuclear transport of the linker histone H1 is mediated by the receptor pair Impß-Imp7 and represents an example for the co-import pathway. Early studies showed that both Impß and Imp7 can interact with H1 directly as well as with each other. The nuclear import of H1 comprises interaction with the nuclear pore complex to pass through the membrane, and RanGTP interaction in the nucleus for cargo release. The relevant sites for protein-protein interaction were revealed previously for Impß and Imp7 as well as the nuclear localization signals of H1. Nevertheless, structural information is lacking. The Impß-Imp7 heterodimer not only imports H1, but also the integrase of human immunodeficiency virus-1 (HIV-1-IN). Thus, solving the structure and understanding the Impß-H1-Imp7 complex in more detail, would be of high medicinal interest. Crystallization attempts of the full-length Impß-H1-Imp7 complex were unsuccessful so far. Therefore, various constructs of *H. sapiens* Impß, *X. laevis* Imp7 and *H. sapiens* H1 were cloned, expressed and purified to reconstitute the heterologous trimeric protein complexes. Almost all Imp7 construct versions tended to precipitate after SUMO tag cleavage or only low protein yields could be gained. Thermofluor shift assay was used to find stable complexes with the highest melting points to increase crystallization probability. Numerous crystallization screens were performed using different trimeric and dimeric complex versions of Impß/Imp7-H1. Crystals of the Impß-H1-C-terminal domain dimeric complex were obtained. The best crystal diffracted to 4 Å resolution and crystal structure solution is still in progress.

P49 Establishment of an MRM assay for the quantification of human Hsp90 and its cochaperones

Sakson, Roman; Wiesner, Jan; Ruppert, Thomas; Mayer, Matthias P.

University of Heidelberg, Germany

Heat shock protein (Hsp) 90 is an essential and ubiquitous molecular chaperone with a diverse set of clients. The fact that many of those clients are oncogenic makes Hsp90 an attractive target for cancer therapy. Cytosolic Hsp90 and its clients are regulated by a complex network of cooperating chaperones and cochaperones such as Hsp70, Aha1, p23, Cdc37 and Hop. Elevated expression levels of Hsp90 and of several cochaperones are associated with poor prognosis in different types of cancer. However, the exact way in which the network between Hsp90 and its cochaperones behaves in cancer cells remains elusive. A comprehensive quantitative dataset containing expression levels of human Hsp90 and various cochaperones for different cell lines of one particular cancer type is not available to date. In this study, we established a targeted mass spectrometric assay called multiple reaction monitoring (MRM) which enables selective, very sensitive and reproducible detection of human Hsp90a- and ß-isoforms, Hsp70, Hsc70 and 14 different cochaperones of Hsp90 in a single measurement. We have also labeled a HepG2 cell line with heavy isotopes using stable isotope labeling by amino acids in cell culture for relative quantification. Preliminary data showed a significantly decreased expression level of Hsp70 in HuH7 cells compared to HepG2 cells, while the expression levels of other monitored proteins remained similar between the two cell lines. The validated MRM assay will now serve as the basis for evaluation of several hepatocellular carcinoma cell lines. The resulting dataset might provide valuable insights into the Hsp90 protein network in the context of one of the most prevalent cancer types worldwide.

P50 Scores for standardization of on-tissue digestion of formalin-fixed paraffin-embedded tissue in MALDI-MS imaging

Sammour, Denis; Erich, Katrin; Marx, Alexander; Hopf, Carsten

Center for Applied Research in Biomedical Mass Spectrometry (ABIMAS), Mannheim University of Applied Sciences, Germany

Today, mass spectrometry imaging (MSI) is being used rigorously in human tissue research in various areas of applications and therefore many tissue preparation workflows and protocols have been suggested and are continuously updated as rapid technical advances in mass spectrometry imaging are being introduced. Several spectral quality scores have been developed to monitor and evaluate these preparation protocols, however, the important notion of reproducibility of the generated data is often overlooked which potentially undermines the possibility of standardized application of matrix-assisted laser desorption/ionization (MALDI) MSI in clinical routine. In this study, we sought to propose several scores for evaluation of homogeneity and reproducibility of on-slide tissue processing and MALDI MSI analysis using five different published FFPE tissue preparation methods with three full technical replicates each applied on two >98% histologically homogeneous human FFPE tissues, gastrointestinal stromal tumor (GIST) and liver. Pixel-wise coefficient of determination and natural fold change scores were introduced for intra- and inter-replicate comparisons for the evaluation of tissue processing homogeneity and method repeatability, respectively. Moreover, scatter-based computational scores were introduced to help numerically compare replicates similarity in principal component analysis (PCA) space. We demonstrated that the suggested homogeneity and reproducibility scores generated different outcomes when applied on the same tissue types which have been processed differently. Moreover, the suggested scatter-based scores proved to be insightful and objective quantitative scores for measuring the similarity of tissue replica in PCA space and therefore can be used for future standardization and quantitative comparison of sample preparation methods for the FFPE tissue.

P51 Deep learning to detect organoids

Sauer, Jan; Fischer, Bernd

German Cancer Research Center (DKFZ), Heidelberg, Germany

The treatment of colorectal cancer is vital to the long-term survival of a patient. The goal of this study is to expand the limited library of pharmaceuticals available to treat colorectal cancer by repurposing or combining compounds released for other indications. Recently, organoids have been found to be useful tools to model organs and study tissue-level phenotypes after drug treatment. High-content microscopy screening of these organoids, after treatment with various compounds, promises to show how new drugs and drug combinations may affect the growth and survival of cancerous cells. The analysis of these microscopy images requires the development of novel software capable of accurately detecting the spheroids in the images. To achieve this, a deep neural network (DNN) is being developed for the feature extraction and subsequent segmentation of the images. This DNN will be able to first find the edges of the organoids and based on this edge map then determine their size. The training of this network will be achieved by a combination of image segments of organoids, which are detected by manually designed filters, as well as an interactive application, which will allow users to annotate microscopy images. Using this segmentation mask, features of individual organoids can be calculated and the effect of various drugs quantified in arbitrary detail.

P52 Cell and nuclear packing during tissue growth

Schienstock, Dominik

The Francis Crick Institute Mill Hill Laboratory, United Kingdom

Tissue development relies on morphogenetic processes that are largely controlled by signalling molecules. Recently it has become clear that morphogenesis and growth are also subject to mechanical feedback operating both at the cellular and tissue level. In my PhD project, I am using *Drosophila* wing imaginal discs, which give rise to the adult wing, as a model to study the growth of tissues. During growth of this tightly packed pseudostratified tissue, cells could exert forces on their immediate neighbours, which in turn is likely to affect growth and other morphogenetic processes. Preliminary results suggest that nuclei decrease in smoothness while increasing in density during the growth of wing imaginal discs. My hypothesis is that nuclear packing (size, shape and position) could be used to infer local mechanical forces such as compression. At the outset of my project, I have developed protocols to image wing imaginal discs at appropriately high resolution while preserving their characteristic shape. I am using a tissue clearing method, agarose embedding and larvae expressing reporters of cell and nuclear membranes. My current aim is to quantify the nuclear packing in 3D as growth of the imaginal discs progresses. My first ambition is to acquire the data and to develop the tools to infer local tissue forces in 3D. This could complement established methods that infer planar forces from the behaviour of apical cell junctions. Secondly, I hope to investigate whether nuclear compression has a functional relevance for gene expression and thus in turn on signalling and growth dynamics.

P53 Temporal and spatial control of fungal filamentous growth

Silva, Patrícia M.; Bassilana, Martine; Arkowitz, Robert A.

Institute of Biology of Valrose - University of Nice, France

The localization of critical activated small Rho-type GTPases coincides with sites of polarized growth or movement in a range of cell types, suggesting that the specific distribution of these molecules may be important for such processes. *Candida albicans* is a harmless commensal fungus that can cause superficial as well as life-threatening systemic infections in immuno-compromised individuals. *C. albicans's* success as a pathogen results from its ability to switch between a budding form and a filamentous hyphal form. The small GTPase Cdc42 is critical for morphogenesis and filamentous growth: it localizes to the plasma membrane and in its active form is enriched in bud and filament tips (1). To determine whether this specific localization is sufficient for morphogenesis, we have targeted activated Cdc42 to the plasma membrane and investigated whether this i) generates new sites of polarized growth; ii) competes with pre-existing sites; iii) induces hyphal tip re-orientation. To specifically recruit activated Cdc42 to the plasma membrane, we are using the blue light-activated cryptochrome system from *A. thaliana* (2). We have fused constitutively activated Cdc42 to one of these plant protein domains and shown that photoactivation results in the recruitment of this fusion protein to the plasma membrane. Such recruitment of activated Cdc42 interferes with the initiation of filamentous growth and the elongation of germ tubes. The extent of interference depends on the amount of activated Cdc42 that is recruited and the length of the germ tubes. Our results demonstrate that the specific localization of activated Cdc42 in *C. albicans* is critical, in time and space, for the initiation and maintenance of filamentous growth.

1. V. Corvest, S. Bogliolo, P. Follette, R. A. Arkowitz & M. Bassilana (2013). Mol. Microbiol. 89: 626-48.2. M. J. Kennedy, R. M. Hughes, L. A. Peteya, J. W. Schwarz, M. D. Ehlers & C. L. Tucker (2010). Nat. Methods 7: 973-975.

P54 The secrets of Munc18 interactions

Sitarska, Ewa

EMBL Heidelberg, Germany

The ability of neurons to communicate with one another via neurotransmitters is absolutely crucial for brain function. Neurotransmitter release is a very well controlled process that involves several steps. This sophisticated machinery consists of many proteins that often have homologues in most types of intracellular membrane traffic. The key players are the SNARE proteins (Syntaxin, Synaptobrevin, SNAP-25), Munc18, Munc13, Synaptotagmin, NSF-SNAP and Complexins. It was thought that the starting point for neurotransmitter release is the syntaxin-SNAP-25 complex, but recent data suggest an alternative model. Two X-ray structures of Vps33 (Munc18 homologue) bound to two SNAREs homologues were reported. When superimposed, the two SNAREs seemed to lay in the correct orientation and register as in the SNARE complex, suggesting that Vps33 and its homologues may act as templates for generating partially zipped SNARE assembly intermediates. The well described interactions of Munc18 are those with syntaxin and the SNARE complex, but not with synaptobrevin. If Munc18 acts as a template for SNARE complex formation, interactions with both syntaxin and synaptobrevin should be crucial. In this study different Munc18 mutants were designed to perturb interactions with synapobrevin. Using Nuclear Magnetic Resonance spectroscopy, we identified a mutation that weakens the Munc18-synaptobrevin interaction, another that strengthens it and another that has no effect. Importantly, these results correlated very well with the effects of the Munc18 mutations in membrane fusion reconstitutions experiments. These results strongly support the notion that Munc18, Vps33 and their homologues function as templates to mediate SNARE complex assembly.

P55 Making nanoscale numbers tangible with 3D printing

Suckale, Jakob

University of Tübingen, Germany

Nanoscale dimensions and depth of biomolecules are notoriously hard to picture. This impedes investigation and learning. We present a protocol to generate accurate, physical three-dimensional models of nanometer complexes using affordable 3D printer to aid research and teaching.

P56 Discrete roles of multiple phosphorylation sites in the Fanconi Anaemia DNA repair pathway

Tan, Winnie; van Twest, Sylvie; Murphy, Vincent; Hodson, Charlotte; Crismani, Wayne; Deans, Andrew

St Vincent's Institute of Medical Research, Australia

Fanconi anemia (FA) is a blood disorder characterized by bone marrow failure, high cancer predisposition and hypersensitivity to DNA cross-linking agents. Patients with FA carry inherited mutations in any one of at least 18 known FA proteins that coordinate function of a DNA repair pathway (the FA pathway). The correct activation of this pathway requires the phosphorylation and ubiquitination of FANCI and FANCD2 proteins. Previous studies suggest that constitutive phosphorylation at multiple FANCI serine residues activates the FA pathway by triggering the monoubiquitination of FANCD2. However, little is known about how FANCI phosphorylation is regulated. We aim to better understand the precise regulation of FANCI phosphorylation in activating the FA pathway, using biochemical reconstitution with recombinant proteins. We prepared recombinant FA core complex, which contains an E3 ubiquitin ligase (FANCL) and five other FA proteins, to examine monoubiquitination of the FANCI:FANCD2 heterodimer *in vitro*. FANCI residues of interest were mutated to alanine (phosphodead) or aspartate (phosphomimic). Biolayer inferometry was used to investigate the influence of chemical modifications of FANCI on FANCD2 binding affinity. We show that phosphomimic mutations at six conserved SQ sites in FANCI caused a significant (1000-fold) (Kd=15.5 µM) decrease in FANCD2 affinity, and the dissociated complex cannot be monoubiquitinated by the FA core complex. Conversely, phosphomimic mutations at one of these serines dramatically increased FANCD2 ubiquitination levels without disrupting the complex (Kd=4.2 nM), suggesting that the phosphorylation of distinct FANCI sites occurs at different steps of FA pathway activation. Our results suggest a novel model of FA pathway activation that involves a dynamic interplay between FANCI phosphorylation and FANCD2 ubiquitination, and reveal that the activation of the FA pathway by FANCI phosphorylation is more complex a process than previously thought.

P59 Mutational signatures of DNA repair deficiencies and cytotoxin exposures in *C. elegans*

Volkova, Nadezda; Meier, Bettina; Gonzalez Huici, Victor; Bertonlini, Simone; Campbell, Peter; Gartner, Anton; Gerstung, Moritz

EMBL-EBI Cambridge, United Kingdom

Cancer is caused by alterations in the genome. These alterations can be an effect of combination of environmental factors damaging DNA and deficiencies in DNA repair and replication leading to characteristic mutational spectra. Mutational signatures (Alexandrov et al. 2013) became a very useful tool of cancer investigation in the last years. However, the signatures identified so far mostly represent complex conglomerates of the action of different mutational processes. For many signatures, the link with the underlying mutational processes is still unclear. In this study we used *C. elegans* as a model organism to present a systematic screen with 9 types of genotoxins under 58 different genetic conditions including single and double knockouts of DNA repair associated genes. Upon exposure over several generations we used whole-genome sequencing to study patterns of DNA damage. We studied the mutational spectra by analysing different types of genetic lesions including point mutations, indels and structural variants using rigorous quality control procedure. This approach allows us to dissect the precise individual contributions of each factor using zero-inflated negative binomial additive models, and also identify significant genetic and gene-mutagen interactions such as 3-fold increase in mutational burden for pms-2/pole-4 double knock-out and mutational spectra expansion for DMS exposure in polk-1 mutants. In summary, this analysis presents the first systematic catalogue of mutational signatures caused by genotoxins and DNA repair deficiencies.

P60 Structural study of the catalytic domain of RNase E

Wandzik, Joanna; Prof. Luisi, Ben; Bandyra, Katarzyna

EMBL Grenoble, France

Ribonuclease E is an enzyme that can internally cleave polymeric ribonucleic acid. It is the main enzyme implicated in metabolism of RNA in bacteria and its substrates belong to distinct RNA families. Cleavage performed by RNase E is observed in processes such as: mRNA degradation, tRNA and rRNA maturation and processing of regulatory sRNA, and sRNA-mediated gene silencing. N-terminal domain (NTD) of RNase E is highly conserved among proteobacteria and is responsible for catalytic activity of the enzyme. RNase E cleaves its substrates in single-stranded regions, but no particular RNA sequence motif, which might guide this cleavage, has been identified. However, recent high-throughput sequencing analysis on transcriptome-wide scale in *E. coli* revealed in many mRNAs which are RNase E substrates the presence of a structural motif upstream of the cleavage site (Del Campo et al, PLOS Genetics, 2015). So far crystal structures were obtained only for NTD of RNase E with shorter unstructured substrates (Callaghan et al, Nature, 2005).Based on the hypothesis that a structural motif might guide cleavage by RNase E, the aim of my master's project was to study the catalytic domain of RNase E in complex with a natural substrate. RprA, a small regulatory RNA, was chosen as a model candidate for the study in complex with RNase E due to the presence of structural motif preceding RNase E cleavage site, which liberates processed form of the sRNA (Papenfort et al, PNAS, 2015). Crystals of the catalytic domain of RNase E and full length, unprocessed RprA were obtained and initial low resolution X-ray crystallography structural data collected. Studies were complemented with RNA degradation and binding assays. The structure gave an insight into interaction surface between the enzyme and a stem-loop present in the substrate upstream of the RNase E processing site, and allowed identification of a domain implicated in potential recognition of structural elements in the RNase E substrates.

P61 Transforming Growth Factor beta-Activated Kinase 1 (TAK1) is a novel target for retinal neovascularisation

Wang, Jiang-Hui; Ling, Damien; Tu, Lei-Lei; van Wijngaarden, Peter; Dusting, Gregory J; Liu, Guei-Sheung

The University of Melbourne, Australia

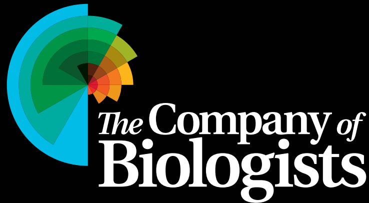
Aim: To investigate whether TAK1 is a suitable therapeutic target in a rat model of oxygen-induced retinopathy. Methods: MiRNA sequencing was performed on retinal RNA isolated from control (normoxic) and rats subjected to oxygen-induced retinopathy (OIR). Bioinformatic analysis was then undertaken to identify candidate pathways and genes involved in retinal neovascularisation. Identified miRNAs and associated candidate genes were then validated by quantitative reverse transcription PCR (RT-qPCR). TAK1 was blocked by a selective TAK1 inhibitor, 5Z-7-oxozeaenol, to assess its potential role in angiogenesis by pro-angiogenesis assays *in vitro* including tube formation, cell proliferation, cell migration and aortic ring assays. The effects of intravitreal injection of 1µM of 5Z-7-oxozeaenol were investigated further in our *in vivo* rat model of retinal neovascularisation induced by OIR. Results: Expression of miRNA143-3p was significantly reduced in OIR rats compared to normoxic controls. TAK1 was identified through bioinformatic analysis as a potential target gene regulated by miRNA143-3p. *In vitro* angiogenesis assays demonstrated that 5Z-7-oxozeaenol can attenuate endothelial cell tube formation, migration and proliferation as well as vascular sprouting from aortic rings. *In vivo*, a significant reduction of retinal neovascularisation was observed in the OIR rat model following a single intravitreal injection of 5Z-7-oxozeaenol. Conclusion: Taken together, these data suggest that TAK1 is involved in development of retinal neovascularisation. TAK1 may represent a suitable target for the development of new therapeutics for retinal neovascularisation in diseases such as proliferative diabetic retinopathy, because it not only contributes to angiogenesis, but also activates inflammatory signals.

P62 Force measurements of single virus particle uptake

Wiegand, Tina; Liu, Yang; Galior, Kornelia; Fratini, Marta; Boulant, Steeve; Salaita, Khalid; Cavalcanti-Adam, Ada

Max Planck Institute for Medical Research, Germany

Mammalian reoviruses bind to host cell surface receptors in order to initialize their internalization. At the cell surface, several adhesion proteins that mediate cell-cell or cell-matrix interactions, such as JAM-A or integrins, facilitate virus entry. While structural and biochemical properties of these interactions have been extensively studied, little is known about the biophysical determinants of viral attachment and entry into the host cell. Adhesion forces mediated by integrins are regulated by receptor lateral clustering and result in functional changes such as differentiation or cell fate. Here we hypothesize that the signaling leading to receptor-mediated endocytosis might be induced by forces that are generated upon viral attachment to cell surface receptors. Further, during the uptake process even higher forces are expected to overcome the bending and tension energy of the cellular membrane of the host cell. To probe the forces between single virus particles and cells at the basolateral side where cell-matrix contacts are formed, we applied single molecular tension fluorescence microscopy. We found that the forces exerted by cells on the surfaces at the sites of viruses overcome the biotin-streptavidin bond used for virus immobilization. Thus, we modified the DNA hairpin sensors and titin-based tension sensors such that virus particles could be covalently immobilized by click chemistry. This method allows to elucidate the role of biomechanical processes between viruses and cells since it provides (i) a detailed analysis of the forces during virus particle uptake and (ii) an insight into the spatio-temporal relation between the localization of endocytotic proteins and forces.



The Company of Biologists is a not-for-profit publishing organisation dedicated to supporting and inspiring the biological community. We are run by distinguished practicing scientists. We exist to profit science, not shareholders. We inspire new thinking and support the worldwide community of biologists.

We do this by publishing leading peer-reviewed journals, facilitating scientific meetings and communities, providing travel grants for young researchers and by supporting societies and facilitating communities.

Grants and Fellowships

We use the surplus we generate for the benefit of biology, supporting and encouraging the sharing of knowledge across the biological community by funding various Grants and Travelling Fellowships.

Visit **www.biologists.com/grants** or **www.biologists.com/travelling-fellowships**

Workshops and Meetings

Through our regular Workshops and Journal Meetings, we help establish and develop professional networks that disseminate knowledge and strengthen personal connections across the scientific community.

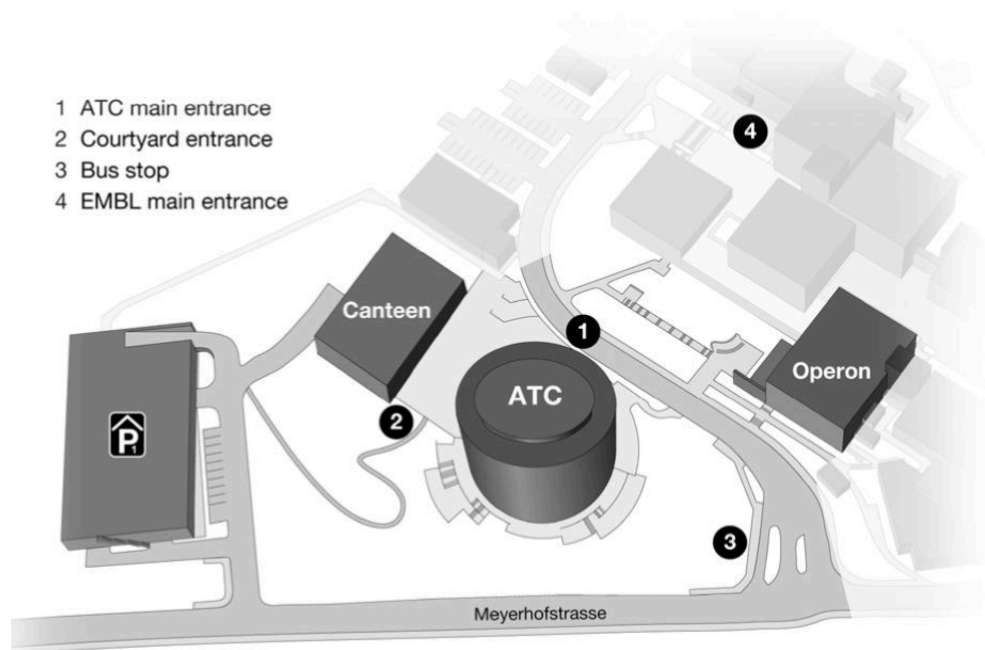
Visit **www.biologists.com/workshops** or **www.biologists.com/meetings**

For more information visit **www.biologists.com**

Development | Journal of Cell Science | Journal of Experimental Biology | Disease Models & Mechanisms | Biology Open

General Information

Map of EMBL Campus



The symposium will take place at the EMBL Advanced Training Centre (ATC).

Health and Safety Notes

Upon arriving please register at the reception where you will be issued a participant badge. While on campus, please wear your conference badge at all time for security purposes.

- Smoking is not allowed anywhere in the buildings.
- Eating and drinking is prohibited in the Auditorium and all laboratories.
- Do not access any laboratories unless you are accompanied, authorized and instructed accordingly.

If first aid is required:

- The first aid room (room 10-205) is located next to the registration desk in the ATC.
- The Emergency number 222 can be dialled from any internal phone. (Where is the accident? What happened? How many injured?)
- All accidents have to be reported to the conference officers at the registration desk.

In case of fire:

Please note that no fire drill is scheduled during this meeting. In the case of fire, a fire alarm will go off and you will be asked to evacuate the building. Follow the escape route and exit signs and proceed to the nearest meeting point. Follow the instructions of the responsible fire wardens on site. Do not re-enter the building until you are told that it is safe.

Getting to EMBL

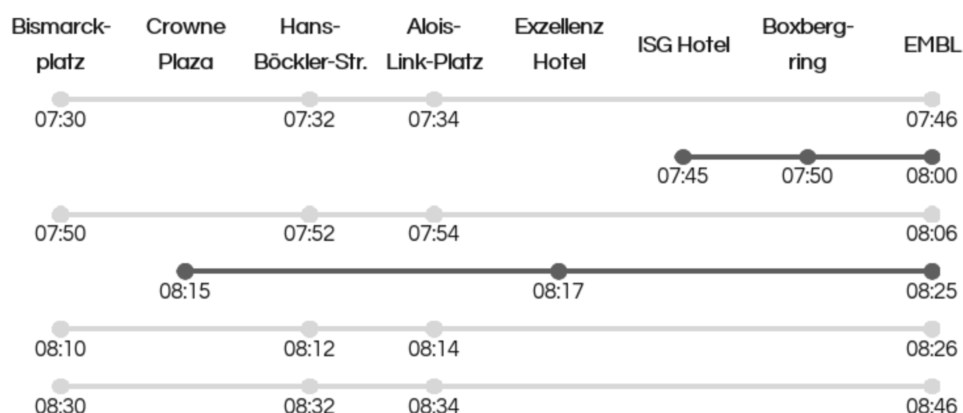
We will provide buses from Heidelberg to EMBL. The bus timetable is provided below.

On Saturday there is no public bus with a direct connection to EMBL. You will have to use the buses provided by us.

● bus provided by EMBL ● bus 39 by RNV (2.50€)

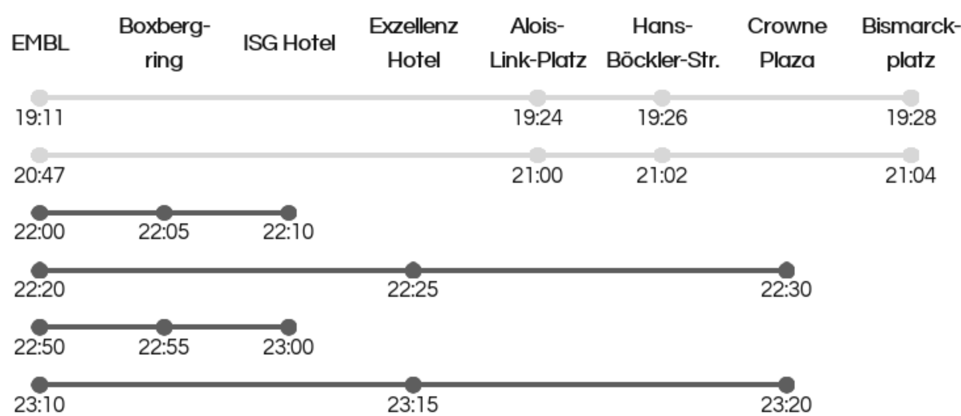
Thursday, November 17th

Bus leaving from **Heidelberg** to **EMBL**



Bismarck-platz	Crowne Plaza	Hans-Böckler-Str.	Alois-Link-Platz	Exzellenz Hotel	ISG Hotel	Boxberg-ring	EMBL
07:30		07:32	07:34				07:46
					07:45	07:50	08:00
07:50		07:52	07:54				08:06
	08:15			08:17			08:25
08:10		08:12	08:14				08:26
08:30		08:32	08:34				08:46

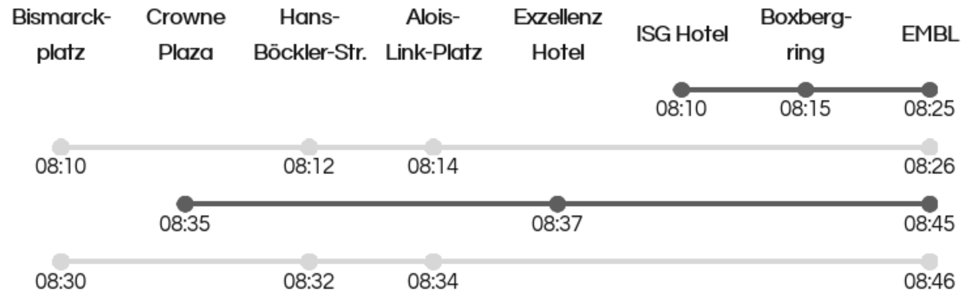
Bus leaving from **EMBL** to **Heidelberg**



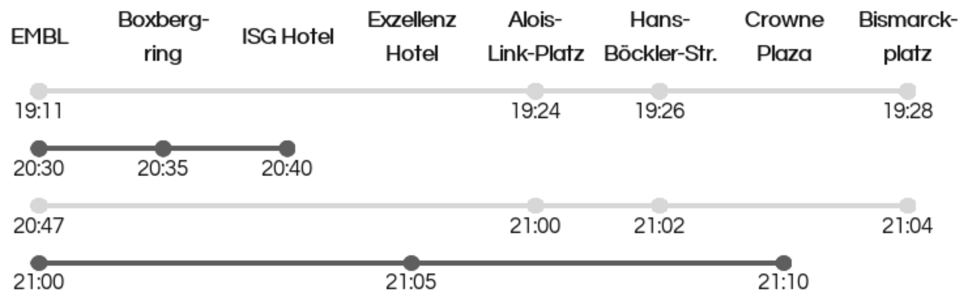
EMBL	Boxberg-ring	ISG Hotel	Exzellenz Hotel	Alois-Link-Platz	Hans-Böckler-Str.	Crowne Plaza	Bismarck-platz
19:11				19:24	19:26		19:28
20:47				21:00	21:02		21:04
22:00	22:05	22:10					
22:20			22:25			22:30	
22:50	22:55	23:00					
23:10			23:15			23:20	

Friday, November 18th

Bus leaving from **Heidelberg** to **EMBL**



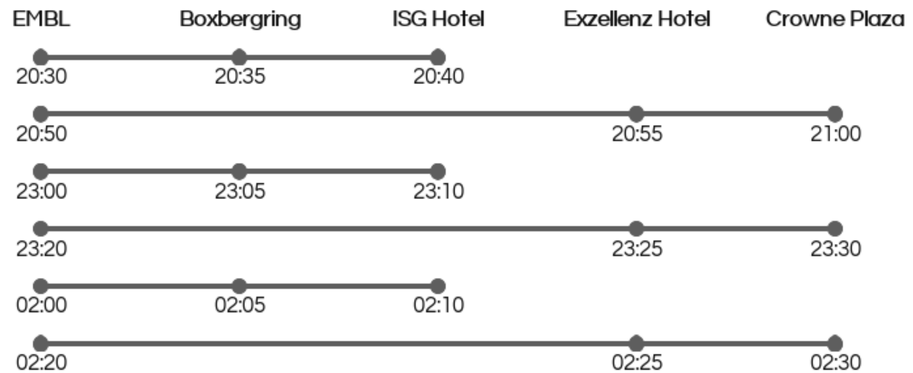
Bus leaving from **EMBL** to **Heidelberg**



Saturday, November 19th

Bus leaving from **Heidelberg** to **EMBL**

Bus leaving from **EMBL** to **Heidelberg**



Public Transportation

Taxi You can call a local taxi on: Taxi Centrale +49 (0) 6221/302030 or we can call one from you from the reception desk.

Car If you are travelling by car we recommend parking in the car park P1, at the beginning of Meyerhofstrasse. The car park is free of charge.
GPS Address: Meyerhofstrasse 1, 69117 Heidelberg

Train For train travel times check the German Rail website. A timetable to Frankfurt International Airport available on the conference is available at the info board.
`http://www.deutschebahn.com/site/bahn/en/start.html`

Individual airport transport We recommend booking in advance your transport back to the airport. Please note that we do not organise individual airport transfers for participants, only for invited speakers.

A&S Airportservice
Tel: +49 (0) 6221-727 44 66
Mobil: +49 (0) 172-7448-856
E-mail: info@as-airportservice.de
www.as-airportservice.de

TLS
Tel: +49 (0) 6221 770-077
E-mail: info@tls-heidelberg.de
https://www.tls-heidelberg.de/home/

Express Drive
Tel: +49 (0) 7223 808-38-90
24h hotline: +49 (0) 172 723-50-50
E-mail: airport@expressdrive.de
www.expressdrive.de

PMJ Fahrservice
Tel: +49 (0) 6223 954-03-65
Mobile: +49 (0) 163 723-23-48
E-mail: info@pmj-fahrservice.de
www.pmj-fahrservice.de

Lufthansa Bus Service The bus runs every 90 minutes, seven days a week between Terminal 1, Arrival Area, Hall B, Exit B4-5, Frankfurt International Airport and downtown Heidelberg Crowne Plaza Hotel, Kurfürstenanlage, Heidelberg (city centre).
You do not need to be a Lufthansa passenger in order to use this service. The shuttle has 8 seats and therefore we recommend early booking in order to reserve a seat. Cost: 24 EUR. A schedule is available at the info board.
http://www.lufthansa.com/online/portal/lh/de/info_and_services/from_to_airport?nodeid=3163691&l=en

Lufthansa Bus Service
Tel: +49 (0) 6152 976-90-99
E-mail: info@pmj-fahrservice.de
www.transcontinental-group.com/en/frankfurt-airport-shuttles

Poster Session Information

During the conference there will be a permanent poster exhibition with 2 sessions of viewing:

Thursday, 17th November, 15:45-16:45, Helix A
Friday, 18th November, 15:15-16:15, Helix A

Your poster board number is the number of your abstract in the abstract book. Please have your poster ready on the poster board on the first day, whatever your session.

Poster boards will be located on Helix A in the Advanced Training Centre. The sizes of our poster boards are 1.05 m wide x 2.30 m high. Our poster boards are made of fabric on a metallic frame. The posters will be fixed with pins. Pins are available on the board. If you need additional pins, please ask at the registration desk. We recommend that you do not bring laminated posters.

Information for Speakers

All talks will be held in the EMBL Advanced Training Centre Klaus Tschira Auditorium. Please get in touch with the audiovisual staff at the back of the Auditorium in advance of the time of your talk. We prefer to have the presentation running on our machines due to incompatibilities that might appear if running from your own workstations. If your presentation contains movies, please save the movie files and the presentation in one folder (with an indication of order). The file name should be labeled with your name and the date that the file was last modified or created.

We ask you to please make sure to keep within your presentation time limit. You can address our AV technician, Sean Nightingale, for help regarding your presentations:

Sean
Nightingale

Catering

All meals and coffee breaks are included in the registration fee. Our catering staff will prepare a wide variety of vegetarian meals, meat and fish dishes, soups, pasta, fresh fruit and vegetables, as well as a variety of desserts. Please wear your badge at all times when serving yourself.

NO FOOD OR DRINKS ARE ALLOWED IN THE AUDITORIUM.

Coffee breaks will take place in the ATC Foyer.
Lunch will be served in the EMBL Canteen.
Dinner will be served in the EMBL Canteen.
The party (Sat. Nov. 19th) will be located in the ATC Foyer.

Questionnaires & Badges

Please help us with the organisation of future conferences by giving us your **feedback** on this meeting. After the meeting we will be sending the questionnaire link per mail to all participants.
Please help us to be green by returning the reusable plastic holder of your badge at the end of the conference at the registration desk.

Photography

During the conference an EMBL Photographer will be taking photographs. If you would not like to appear in these, please inform the photographer or a member of the Course and Conference Office.

EMBL Merchandise

EMBL Merchandise is available during weekdays (during office hours). If you are interested in purchasing an EMBL souvenir (products presented in the glass display in the registration area), please ask at the registration desk for more information.

Useful Telephone Numbers

Internal Numbers:

EMBL's Advanced Training Centre registration desk 8752
Course & Conference Office 8625 / 8797
Switchboard/Security 8100
Ambulance 112

Conference Telephone Fax & E-mail

The conference telephone number where you can be reached or where messages can be left for you is: +49 6221 387 8752.

The conference fax number is: +49 6221 387 8158. Faxes or messages will be posted on the info board near the registration desk.

WiFi is available everywhere on the premises (no password required, just register as an ATC Guest). Computers with internet access where you can access your e-mails are located in the E-Lounge at the beginning of Helix A. (room A0402)

Contact

If you have any further questions please contact the conference officer at the registration desk. There will be a member of the conference office at the registration desk throughout the entire conference.

Tourist Information

There is a map with points of interest online: http://binged.it/1KXfwHc

HEIDELBERG ALTSTADT

The Heidelberg Tourist Office (Located at Heidelberg Hauptbahnhof) puts on tours of the old town that take you to the points of interest in about 2 hours. The old town does not cover a particularly large area - the best starting point for your exploration is probably Bismarckplatz. From there, you can walk down Hauptstraße (1.6 km long). This is the main shopping street in Heidelberg. The pedestrian part of Hauptstraße ends on Kornmarkt from where you can walk up to Heidelberg castle. Alongside Hauptstraße you can find these interesting places:

- Universitästplatz and the old lecture hall (Alte Aula): Beautiful wood carvings and decorations inside the old lecture hall
- Student prison (Studentenkarzer) in Augustinergasse: the prison is full of graffiti and writings from students who have been arrested there during the last 2 centuries.
- Jesuitenkirche (Jesuit's church) on Schulgasse
- Kornmarkt: beautiful view of the Castle
- Marktplatz: great for a coffee in the sun
- Heiliggeistkirche (Holy Ghost church) on Marktplatz: Gothic church
- Heidelberger Zuckerladen: great sweet shop in Plöck 60
- Alte Brücke (Old Bridge): 250 years old stone bridge
- Philosophenweg: short walk up the hill with a great view of the old town and castle

HEIDELBERG CASTLE / CASTLE GARDENS

The beautiful old castle dominates the Heidelberg skyline, looming over the old town. Once inside the Castle courtyard, you will see quite clearly that parts of the castle were built at different times in different styles. In the cellar you can find the Grosses Fass (Big Barrel)- the biggest wooden barrel ever to have been filled with wine. It was constructed in 1751 and can hold over 221,000 liters! There is a little walkway which takes you across the top of the barrel. Do not forget to see the old pharmacy museum and the historical pharmacy laboratories. Make sure you go out onto the Belvedere terrace you will be rewarded with great views of the old town below. The castle gardens are always open.

WHERE TO GO OUT IN HEIDELBERG

For food or a casual drink

Café Rossi Rohrbacher Straße 4, 69115 Heidelberg
A wide selection of international food and drinks, very nice brunch on Sundays. Good and cheap coffee at the bar.

Hemingway's Fahrtgasse 1, 69117 Heidelberg
Nice, friendly atmosphere with American fast food style food. It has a small beer garden, which is popular in summer and in winter, since they have outdoor heaters. It overlooks the Neckar.

O'Reilley's Brückenkopfstraße 1, 69120 Heidelberg
Irish bar with pub quiz on Monday night. Shows Rugby and football, live music on some nights and does a fantastic fry-up and Sunday lunch.

Schnitzelhaus "Alte Münz" Neckarmünzgasse 10, 69117 Heidelberg
A small old-german style restaurant: A 100 different schnitzel, but only 1 vegetarian dish.

For real drinks and Party

Destille Untere Straße 16, 69117 Heidelberg
Most famous bar in Heidelberg. Get their Heidelberg triple: Melon schnaps, Gehängter and a Warmer Erpel to round it up. The right mix to end up in the next destination on the list!

Cave54 Kramergasse 2, Heidelberg
Legendary "club" every party ends up going. If you have been (drinking) in Heidelberg and haven't been here, you haven't been in Heidelberg properly.

Dubliners Hauptstrasse 9, Heidelberg
They have a selection of Irish ciders. Football and rugby games are shown and it turns into a club at the weekends after midnight.

Orange Ingrimstraße 26, 69117 Heidelberg
Cool but small bar in the middle of the little streets in old town, not to far away from Cave54

Vetter Steingasse 9, 69117 Heidelberg
Old brewery next to the Old Bridge. Good self-brewed beer and a good hearty dinner until midnight. Even people who dislike beer, might find themselves one they are able to tolerate here

Participants

Yevhen Akimov
Institute for Molecular Medicine Finland, Helsinki, Finland

Cassie Albury
Queensland University of Technology, Brisbane, Australia

Ashna Alladin
EMBL Heidelberg, Germany

Renato Alves
EMBL Heidelberg, Germany

Tivkaa Amande
University of Essex, Colchester, United Kingdom

Ricard Argelaguet
EMBL-EBI Cambridge, United Kingdom

Alexander Aulehla
EMBL Heidelberg, Germany

Chiara Baccin
EMBL Heidelberg, Germany

Zsolt Balázs
University of Szeged, Hungary

Kim Bartels
EMBL Hamburg, Germany

Kolja Becker
Institute of Molecular Biology Mainz, Germany

Maximilian Beckers
EMBL Heidelberg, Germany

Ivan Berest
EMBL Heidelberg, Germany

Benedikt Best
EMBL Heidelberg, Germany

Meriam Bezohra
EMBL Heidelberg, Germany

Jacob Bobonis
EMBL Heidelberg, Germany

Tom Boissonnet
EMBL Monterotondo, Italy

Matthew Boucher
EMBL Heidelberg, Germany

William Bradshaw
Max Planck Institute for Biology of Ageing, Köln, Germany

Annika Brosig
EMBL Heidelberg, Germany

Magdalena Büscher
EMBL Heidelberg, Germany

Jelena Calyseva
EMBL Heidelberg, Germany

Nikeisha Caruana
La Trobe University, Melbourne, Australia

Lucia Cassella
EMBL Heidelberg, Germany

Gabriel Cavalheiro
EMBL Heidelberg, Germany

Himanshu Chheda
University of Helsinki, Finland

Jason Cosgrove
University of York, United Kingdom

Chiara Cotroneo
University College Dublin, Ireland

Tom Crosskey
EMBL Hamburg, Germany

Anna Cuomo
TU Delft, The Netherlands

Hannah Currant
EMBL-EBI Cambridge, United Kingdom

Jakub Czuchnowski
EMBL Heidelberg, Germany

Svend Dahl-Jensen
Center for Stem Cell Decision Making (StemPhys), Copenhagen, Denmark

Peter de Peinder
VibSpec, Utrecht, The Netherlands

Handan Melike Dönertas
Middle East Technical University, Ankara, Turkey

Corina Duenas
EMBL-EBI Cambridge, United Kingdom

Nguyet Duong
The University of Western Australia, Perth, Australia

Éric Durandau
Université de Lausanne, Switzerland

Theocharis Efthymiopoulos
EMBL Heidelberg, Germany

Nils Eling
EMBL-EBI Cambridge, United Kingdom

Buesra Erarslan
EMBL Heidelberg, Germany

Cihan Erkut
EMBL Heidelberg, Germany

Miriam Fontanillo
EMBL Heidelberg, Germany

Christoph Fritzsch
Institute of Molecular Biology Mainz, Germany

Sarah Noel Galleguillos
Austrian Centre of Industrial Biotechnology, Wien, Austria

Elisa Gallo
EMBL Heidelberg, Germany

Charlotte Gehin
EMBL Heidelberg, Germany

Maja Gehre
EMBL Heidelberg, Germany

Raymond E. Goldstein
University of Cambridge, United Kingdom

Ivan Golushko
Université de Montpellier, France

Kristján Grétarsson
EMBL Monterotondo, Italy

Adam Gristwood
EMBL Heidelberg, Germany

Matteo Guerra
Parma University, Italy

Moshir Harsh
EMBL Heidelberg, Germany

Jonas Hartmann
EMBL Heidelberg, Germany

Shabbeer Hassan
Institute for Molecular Medicine (FIMM), Helsinki, Finland

Kevin Haubrich
EMBL Heidelberg, Germany

Sebastian Henkel
EMBL Heidelberg, Germany

Jean-Karim Hériché
EMBL Heidelberg, Germany

Claudia Hernandez
EMBL-EBI Cambridge, United Kingdom

Christine Ho
EMBL Heidelberg, Germany

Russ Hodge
Max Delbrück Center for Molecular Medicine, Berlin, Germany

Bernhard Hoermann
EMBL Heidelberg, Germany

Jan-Erik Hoffmann
EMBL Heidelberg, Germany

Nele Hollmann
EMBL Heidelberg, Germany

Philipp Höß
EMBL Heidelberg, Germany

Dagmar Iber
ETH Zürich, Switzerland

Aleksander Jankowski
EMBL Heidelberg, Germany

Cosimo Jann
EMBL Heidelberg, Germany

Simon Jarrett
University of York, United Kingdom

Pauline Juyoux
EMBL Grenoble, France

Eleni Kafkia
EMBL Heidelberg, Germany

Sravya Kantamneni
EMBL Hamburg, Germany

Eva-Lotta Käsper
EMBL Heidelberg, Germany

Paul Kennouche
Institut Pasteur, Paris, France

Elissavet Kentepozidou
EMBL-EBI Cambridge, United Kingdom

Jeong Yoon (Esther) Kim
EMBL Heidelberg, Germany

Ana Kojic
EMBL Heidelberg, Germany

Christoph Kommer
German Cancer Research Center (DKFZ), Heidelberg, Germany

Dimitrios Konstantinidis
EMBL Heidelberg, Germany

Kevin Koo
Australian Institute for Bioengineering & Nanotechnology, Brisbane, Australia

Verena Körber
German Cancer Research Center (DKFZ), Heidelberg, Germany

Sandra Kozak
EMBL Hamburg, Germany

Tadek Krassowski
University College Dublin, Ireland

Dimitri Kromm
EMBL Heidelberg, Germany

Piotr Krzywkowski
EMBL Monterotondo, Italy

Sergio Lembo
EMBL Heidelberg, Germany

Benjamin Lenzen
Humboldt University of Berlin, Germany

Olivia Liebler
The Art of the Cell, Guilford, United States of America

John Liebler
The Art of the Cell, Guilford, United States of America

Liyan Liu
The University of Melbourne, Australia

Maria Jose Lopez Iniesta
Universitat de Barcelona, Spain

Tomi Määttä
EMBL Heidelberg, Germany

Daniel Machado
EMBL Heidelberg, Germany

Jakub Macosek
EMBL Heidelberg, Germany

Lakshminarayanan Mahadevan
Harvard University , Cambridge, MA, United States of America

Oleksandr Maistrenko
EMBL Heidelberg, Germany

Karen Katrina Manalastas
EMBL Hamburg, Germany

Daniel Elias Martin Herranz
EMBL-EBI Cambridge, United Kingdom

Irene Miguel-Aliaga
Imperial College London, United Kingdom

Sofya Mikhaleva
EMBL Heidelberg, Germany

Alessio Milanese
EMBL Heidelberg, Germany

Enric Mila Vilalta
EMBL Heidelberg, Germany

Heloisa Milioli
The University of Newcastle, New Lambton, Australia

Andreas Mock
EMBL Heidelberg, Germany

Katrin Möller
EMBL Heidelberg, Germany

Jack Monahan
EMBL-EBI Cambridge, United Kingdom

Chiara Morelli
EMBL Monterotondo, Italy

Alexey Morgunov
MRC Laboratory of Molecular Biology, Cambridge, United Kingdom

Robin Muench
EMBL Heidelberg, Germany

Prashant Muraleedharnnair
James Cook University, Townsville, Australia

Walter Muskovic
Children's Cancer Institute Australia, Sydney, Australia

Øyvind Ødegård
EMBL Heidelberg, Germany

Samuel Pažický
EMBL Hamburg, Germany

Lucas Pelkmans
Institute of Molecular Life Sciences, University of Zürich, Switzerland

David Alejandro Peña Navarro
University of Natural Resources and Life Sciences, Vienna, Austria

Leïla Perié
Institut Curie, Paris, France

Umberto Perron
EMBL-EBI Cambridge, United Kingdom

Julia Peukes
EMBL Heidelberg, Germany

Margaux Phares
EMBL Heidelberg, Germany

Paola Picotti
ETH Zürich, Switzerland

Erica Ponzi
University of Zurich, Switzerland

Claudia Proemper
Biotrend Chemikalien GmbH, Cologne, Germany

David Puga
EMBL Heidelberg, Germany

Guillermo Ramirez-Santiago
Universidad Nacional Autonoma de Mexico, Mexico

Luca Rappez
EMBL Heidelberg, Germany

Balaguru Ravikumar
Finland Institute of Molecular Medicine, Helsinki, Finland

Christopher Reinkemeier
EMBL Heidelberg, Germany

Leonie Ringrose
IRI Life Sciences, Berlin, Germany

Carlos Rojas Cordova
EMBL Heidelberg, Germany

Benjamin Roques
UCD, Dublin, Ireland

Tim Rozday
University of York, United Kingdom

Mariana Ruiz Velasco
EMBL Heidelberg, Germany

Luigi Russo
EMBL Heidelberg, Germany

Allyson Ryan
EMBL Heidelberg, Germany

Timothy A. Ryan
Weill Cornell Medical College, New York, United States of America

Roman Sakson
University of Heidelberg, Germany

Hugo Samano-Sanchez
EMBL Heidelberg, Germany

Denis Sammour
Mannheim University of Applied Sciences, Mannheim, Germany

Paul Gerald Sanchez
EMBL Heidelberg, Germany

Jan Sauer
German Cancer Research Center (DKFZ), Heidelberg, Germany

Tim Schendzielorz
University of Heidelberg, Germany

Dominik Schienstock
The Francis Crick Institute Mill Hill Laboratory, London, United Kingdom

Isabell Schneider
EMBL Heidelberg, Germany

Samantha Seah
EMBL Heidelberg, Germany

Luis Serrano
Centre for Genome Regulation, Barcelona, Spain

Olga Sigalova
EMBL Heidelberg, Germany

Patrícia M. Silva
University of Nice, France

Amit Singh
Australian National University, Canberra, Australia

Sanjana Singh
EMBL Heidelberg, Germany

Ewa Sitarska
EMBL Heidelberg, Germany

Naomi Sophie Stierle
EMBL Heidelberg, Germany

Lina Streich
EMBL Heidelberg, Germany

Jakob Suckale
University of Tübingen, Germany

Anna Sueki
EMBL Heidelberg, Germany

Winnie Tan
St Vincent's Institute of Medical Research, Carlton, Australia

Jervis Thevathasan
EMBL Heidelberg, Germany

Sergio Triana
EMBL Heidelberg, Germany

Erika Tsingos
University of Heidelberg, Germany

Andrew Tuckwell
EMBL Australia UNSW, Sydney, Australia

Lara Urban
EMBL-EBI Cambridge, United Kingdom

Lea Urpa
Institute for Molecular Medicine, Finland (FIMM), Helsinki, Finland

Britta Velten
EMBL Heidelberg, Germany

Carina Vibe
EMBL Heidelberg, Germany

Ambra Villani
EMBL Heidelberg, Germany

Ranjith Viswanathan
EMBL Heidelberg, Germany

Dimitrios Vitsios
EMBL-EBI Cambridge, United Kingdom

Anastasiia Vlasiuk
TU Dresden, Germany

Harald Vöhringer
EMBL-EBI Cambridge, United Kingdom

Nadezda Volkova
EMBL-EBI Cambridge, United Kingdom

Sibylle Vonesch
EMBL Heidelberg, Germany

Joanna Wandzik
EMBL Grenoble, France

Jiang-Hui Wang
The University of Melbourne, East Melbourne, Australia

Tina Wiegand
Max Planck Institute for Medical Research, Heidelberg, Germany

Felix Williams
EMBL Heidelberg, Germany

Manli Yang
University Wuerzburg, Germany

Klaus Yserentant
University of Heidelberg, Germany

Iskander Zharkenov
FIMM, Helsinki, Finland

Christian Zimmerli
EMBL Heidelberg, Germany

Notes

Notes

Notes

Notes