CBG Postdoc Retreat 2018

Monday 11 June 2018 - Wednesday 13 June 2018

Palace Brunow, Poland

Book of Abstracts

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Session I / 16

The rise and fall of microglia regulating central nervous system regeneration

Veronique Miron[1]

[1] *Queen's Medical Research Institute, University of Edinburgh, Edinburgh*

Veronique Miron did her PhD at McGill University in Montreal under the supervision of Dr. Antel and Dr. Kennedy. After graduating in 2009, she continued in the group of Dr. Antel as Postdoctoral Fellow. In 2010 she moved to the Medical Research Council Center for Regenerative Medicine at the University of Edinburgh. She stayed until 2013 in the groups of Prof. Ffrench-Constant and Prof. Franklin. In January 2014 Veronique Miron started her own lab in Edinburgh as Principal investigator/Assistant Professor at the Queen's Medical Research Institute.

Career advice:

• **Be pro-active:** present your work whenever you can, speak to people at conferences, ask for advice on your work, meet with invited speakers, submit funding applications (even if for small amounts). This is all networking that could lead to professional opportunities.
• **Finesse presentation skills**: Give practice presentations, read successful and unsuccessful funding bids, learn to draw your own diagrams to convey your message or hypothesis in a clear simplified way. I recommend the e-book '4 Steps to funding' by Morgan Giddings for a template for the order to present your ideas, and the software BioRender for easy diagram making (even if you are artistically challenged!).
• **Find your niche:** think about what you want to be known for, what gap you are filling in scientific knowledge that will be your specialty and the pitch you use in grant/job applications. e.g. I want to be the 'microglia and regeneration' person. You would then select activities or direct your pitch towards this in talks, applications, etc. to be known for this 'thing'. It could be an area of research, an approach, a technique, anything that sets you apart from the crowd.

Abstract:

The prime example of effective regeneration in the central nervous system is that of remyelination, whereby re-enstheathment of axons with myelin restores electrical impulse conduction and trophic/ metabolic support. Remyelination fails in a multitude of neurological disorders, which is considered to contribute to the axonal damage/ loss correlating to clinical decline. The lack of approved therapies promoting remyelination highlights the need to elucidate the underpinning mechanisms. Our previous work showed that efficient remyelination requires dynamic regulation of microglia activation, with a transition from a pro-inflammatory (iNOS+ TNF-alpha+ CD16/32+) to regenerative phenotype (Arg-1+ CD206+ IGF-1+) needed to initiate remyelination. The chronic pro-inflammatory microglia activation commonly observed in neurological disorders suggests an impairment in this transition. However, the cellular and molecular mechanisms regulating the activation of microglia and resolution of inflammation are unknown. Using a combination of ex vivo and in vivo modelling of myelin damage, live imaging of microglia dynamics, and correlation to human CNS pathology, we have unveiled hitherto unrecognized cellular and molecular events that control microglia activation and remyelination. We believe that these reveal novel therapeutic strategies to dampen CNS inflammation-associated pathology and support a regenerative response to reinstate neural health.

Session I / 1

Like mother, like child…how extrinsic factors influence neurogenesis.

Barbara Krystyna Stepien[1]

[1] *MPI-CBG*

Despite similar brain organization mammals present with a variety of neocortex sizes, which are generated during a short developmental window in embryogenesis. The final neuronal output is determined by the initial pool size and proliferative capacity of various cell lineages as well as by the length of the neurogenic period.
In our study we explore the previously proposed link (Lewitus et al., 2014) between the neurogenic period and gestation length in a mouse model system. We use mouse strains with genetically different gestation length to determine the number of produced neocortical neurons in relation to the length of this developmental period. The long-gestation strain produces more cortical layer neurons belonging specifically to the upper but not lower layers. Moreover, the onset of gliogenesis, which in mouse follows the neurogenic period, appears later in this strain suggesting the lengthening of the neurogenic period. This effect depends on the maternal environment as embryo transfer between the short- and long-gestation strains equalizes neuron production consistent with maternal phenotype.
Our results point to a common developmental mechanism synchronizing gestation with neurogenic period and suggest an important role of maternally-derived factors in determining the final neocortex size.

Session II / **15**

Order in disorder revealed by evolutionary couplings

Agnes Toth-Petroczy[1]

[1] *MPI-CBG, CSBD*

Ágnes Tóth-Petróczy did her PhD, at the Weizmann Institute of Science, Rehovot, Israel. She studied the paths of evolving protein sequences under the supervision of Prof. Tawfik. In 2014, she moved to Harvard University in Boston to start a postdoctorat in the group of Prof Marks. As postdoctoral research fellow, she studied the structured states of disordered proteins from genomic sequences. From 2016 to 2018 Ágnes Tóth-Petróczy was a Bioinformatic Case Analyst at Brigham Genomic Medicine (Harvard Medical School and Brigham and Women's Hospital). Since April 2018 she is a Research Group Leader at MPI-CBG.

Career advice:

Cartoon caption: "Do you need to be a superwoman to do it all? NO. Just prioritise, compartmentalise your time, and outsource what is not fun."

Abstract:

Protein flexibility ranges from simple hinge movements to functional disorder. Around half of all human proteins contain apparently disordered regions with little 3D or functional information, and many of these proteins are associated with disease.
Building on the evolutionary couplings approach previously successful in predicting 3D states of ordered proteins and RNA, we developed a method to predict the potential for ordered states for disordered proteins with sufficiently rich evolutionary information.
The approach is highly accurate (79%) for residue interactions as tested in more than 60 known disordered regions captured in a bound or specific condition. Assessing the potential for structure of more than 1,000 apparently disordered regions of human proteins reveals a continuum of structural order with at least 50% with clear propensity for three- or two-dimensional states. Co-evolutionary constraints reveal hitherto unseen structures of functional importance in disordered proteins.

Session II / **12**

Studying genomic changes in mammals shaped by the evolution of distinct phenotypic traits

Nikolai Hecker[1]

[1] *MPI-CBG, CSBD*

Changes in mammalian genomes reflect the evolution of distinct phenotypic traits. For instance, these phenotypic traits comprise adaptations to different habitats, diets, and morphological changes. Such changes can lead to the loss of protein-coding genes that do not serve advantageous or essential functions for the corresponding species. Our group previously developed a method for accurately detecting in-activating mutations in protein-coding genes, which render a protein-coding gene non-functional, referred to as gene loss. Using a forward genomics principle combined with selection rate analysis, we identified gene losses in independent lineages that relate to the convergent evolution of phenotypic traits. In this context, we identified gene losses related to the transition to an aquatic environment, the loss of tooth enamel and an herbivorous or carnivorous diet. Morphological traits such as the absence of specific bones, however, are less likely to be reflected by gene loss, but are more likely to exhibit changes in non-coding gene regulatory elements. To address this aspect, we computed an alignment of 120 mammalian genomes specifically geared towards an improved coverage of non-coding elements. This 120way genome alignment allows us to study genomic changes related to a wide-range of morphological traits over a broad phylogeny of mammalian species.

Session II / **4**

The tight junction plague a dynamic condensate for sequestering effector proteins.

Oliver Beutel[1] ; Chen-Ho Wang[1] ; Karina Pombo-Garcia[1] ; Riccardo Maraspini[1] ; Yara Alcheikh[1] ; Oscar Alf Honigmann[1]

[1] *MPI-CBG*

Tight junctions form a border between the apical and basolateral plasma-membrane domains and are linked to the machinery that controls apicobasal polarization. This achieved by adhesion/polymerization of the claudin protein family and the interactions with the scaffold proteins on the cytoplasmic side. The main proteins family in the scaffold is the MAGUK family, especially the zona occludens proteins (ZO) which play a key role in the tight junction formation and establishment cellular polarity but it is still unclear how the ZO proteins are involved in this process. We discovered a possible molecular basis of tight junction formation and sequestering of interaction partners to the tight junction. We could show ZO proteins can undergo condensation into dynamic liquid condensates in vitro and in vivo. This condensed ZO scaffold recruits efficiently interaction partners via ZO multiple protein-protein interaction domains which have a low affinity towards their interactions partners. Our findings provide a new molecular function inside for the complex structure of ZO-proteins. It can explain the supra-molecular structure and function of the tight junction as a self-organization process which has a direct impact in the role of the tight junction in cell polarity.

Session II / **17**

Resolving the spatiotemporal map of the tight junction interactome

Karina Pombo Garcia[1]

[1] *MPI-CBG*

Epithelial cell polarization is a fundamental organizing principle during early embryonic development, and later differentiation into specific tissues and organs. It is known that epithelial transition involves asymmetry, where cells polarize into apical, lateral, and basal plasma membrane domains. However, how the identity of the polarized membrane is established and communicated to the transcription machinery within the nucleus? Answering these fundamental questions in biology requires

development of new tools that will allow us to systematically map the molecular interactions at the cell-cell junctions (tight junctions) during the establishment of epithelial polarity.To overcome this, I am developing a novel proteomic based chemical tool to spatiotemporally map the protein and lipid interaction networks of polarized cell membrane domains in living cells. Combining the state-of-art biorthogonal click chemistry with APEX2 we can identify and purify with high specificity the interactome of the proteins genetically tagged with the tool. This approach provides us with a quantitative picture of where and when adhesion, polarity, and transcription proteins interact during the tissue formation process. Together with quantitative and super-resolution microscopy of three-dimensional cell culture, will allow us to develop a mechanistic understanding of how the polarization network stablishes and how it feeds back to cell fate.

Session III / **9**

Precise and efficient editing of mammalian genomes for therapeutic purposes. How synthetic biology will impact therapies of the future?

Marc Güell[1]

[1] *Pompeu Fabra University, Barcelona*

Marc Güell did his PhD in the Group of Dr. Serrano at Center for Genomic Regulation in Spain. In January 2011, he started as a Postdoctoral fellow at "Harvard Molecular Technology Group & Lipper Center for Computational Genetics" under the supervision of Dr. Church. From 2015 to 2016, he was a Wyss Technology Development Fellow at the Wyss Institute, Harvard University. Since spring 2017, Marc Güell is a Tenure track Professor of Synthetic Biology and principal investigator of the group "translational Synthetic Biology" at the Pompeu Fabra University, Barcelona.

Career advice:

Three key aspects for success in science are **creativity, impact and connection-to-society.**

• Think differently. Cultivate your imagination, basic science knowledge, inspiration from other disciplines (art, philosophy, design, …).
• Self-evaluate based in 'outcomes' and less in 'outputs' (number of citations vs number of publications; number of licenses/companies created vs number of patents; …).
• Extend yourself beyond own lab (collaborators, clinicians, industry, patient associations, social outreach, etc…).

Abstract:

One of the most advanced sequencing machines can sequence a human genome in hours but synthesizing ~30% of the yeast chromosome has taken years by a consortium of scientists. We are experiencing a growing gap between our capabilities to read and write DNA. This enormous sequencing capacity made the identification of alleles associated with biological processes easier than ever. However, the pace at which these alleles can be tested in the laboratory or addressed clinically has been limited. Advancement of gene synthesis and development of gene editing techniques increase to our ability to write DNA. Despite important progress, mammalian genome editing is still faces important challenges. Homology driven repair methods are still remarkably inefficient for most primary tissues or large edits, and integrative gene delivery methods such as transposases and lentiviruses cannot control insertion sites. Higher precision and efficiency in primary tissues or 'in vivo' genome editing is required to accelerate basic research and therapeutic translation.

Session III / **23**

Elevator Pitch Session

Session IV / 21

Integrating forces and signalling for cell polarity and migration

Alba Diz-Muñoz[1]

[1] *Cell Biology and Biophysics Unit - European Molecular Biology Laboratory (EMBL), Heidelberg*

Alba Diz-Muñoz did her PhD as a joint grad student in the laboratories of Dr. Paluch and Dr. Heisenberg at the MPI-CBG in Dresden. After her PhD, she continued in the group of Dr. Paluch as Postdoctoral Fellow. In 2012, she moved to California and did her postdoctoral studies with the groups of Dr. Weiner at the University of California San Francisco (UCSF) and Dr. Fletcher at UC Berkeley. Since spring 2016, Alba Diz-Muñoz is a Research Group Leader at the EMBL in the Cell Biology and Biophysics Unit, in Heidelberg.

Career advice:

5 take home messages I gave during the PhD ceremony apply at any career stage so here they are:
• Go on an adventure and pick a challenging project, those are the worthy ones. At the overlap between scientific disciplines there is a lot of cool science to be discovered.
• Be curious
• Pick good mentors, they might just save you from embarrassment when you get a job interview
• Remember that self doubt is a sign of wisdom but don't let it put you down for too long.
• Try! you might just be surprised!

Abstract:

Cells are now broadly appreciated to be mechanical as well as biochemical systems. They generate, transmit, and respond to forces through an intricate network of mechanical components, resulting in cell movement and shape change, as well as altered signalling, modulated expression, and even genomic damage. Contributions to cell mechanics from molecular motors, cytoskeletal filaments, and mechanosensitive proteins have received significant attention, and the cell surface – comprising the plasma membrane and underlying cortical cytoskeleton – has emerged as a unique mechanical system capable of exerting both local and global control of cell form and function. The physical properties of the cell surface can be rapidly modulated, enabling cells to generate or accommodate changes in shape.

Here, I will present our work on the role of membrane-to-cortex attachment in the control of directional persistence during mesendodermal cell migration during zebrafish development, and show that neutrophil migration requires inhibition of actin polymerization via PLD2 and mTORC2 downstream of changes in membrane tension.

Session IV / 11

Patterning the vertebrate retina: How random cell behavior gives rise to an orderly structure

Rana Amini[1] ; Caren Norden[1]

[1] *MPI-CBG*

In the retina, like in most other brain regions, different neuron types are precisely arranged into distinct layers giving the tissue its stratified pattern. Such spatial patterning needs to be highly controlled and orchestrated, as its disorganization leads to impaired retinal function. Yet, how retinal neuron pattern formation emerges remains largely unknown. To understand this, we use the zebrafish retina as a model and study emergence of Horizontal Cell (HC) patterning. Using light-sheet microscopy imaging, we extracted single cell behavior of HCs in the developing retina and found that HC migration patterns, cell-cycle and division kinetics are not stereotypic. Moreover,

our preliminary data showed that HCs send dynamic apical protrusions before migrating apically. This argues that HCs might actively sense and respond to environmental cues and do not exclusively follow intrinsically imprinted migration patterns. To examine this possibility, using a combination of genetic interference and enzymatic digestion assays, we are currently examining how changes in the overall retinal architecture could influence emergence of HC patterning. Together, this work will contribute to our understanding of how well-defined forms and patterns within tissues emerge from cell-tissue interactions during development.

Session IV / 26

Numerical simulations of three-dimensional tissues using Voronoi diagrams, and application to liver development

Quentin Vagne[1]

[1] *MPI-CBG, CSBD*

The liver has a complex organization spanning multiple length-scales. At a small enough scale, it ultimately consists of a network of blood vessels (sinusoids) and a network of bile channels (canaliculi), separated by hepatocytes that must filter the blood from the sinusoids and secrete bile into the canaliculi. The tissue adopts a unique three-dimensional organization in which hepatocyte polarity is very different from the one observed in traditional epithelial tissues. Through theoretical modelling and analysis of experimental data, my goal is to uncover the fundamental mechanisms behind such an organization. Because the liver tissue is inherently three-dimensional, it requires new three-dimensional simulation methods. I will show how, using Voronoi diagrams, one can efficiently generate complex three-dimensional tissues in a computer, and I will present how to use this method in the case of the liver.

Session IV / 10

Polynucleotide kinase phosphatase (PNKP) in neuropathological diseases

Ilona Kalasova[1] ; Hana Hanzlikova[2] ; Keith Caldecott[2]

[1] *Institute of Molecular Genetics of ASCR v. v. i, Prague, Czech Republic*

[2] *Institute of Molecular Genetics of ASCR v. v. i, Prague, Czech Republic; Genome Damage and Stability Centre, University of Sussex, Falmer, Brighton, UK*

DNA is a target of various damaging agents such as reactive oxygen species, ionizing radiation, or abortive topoisomerase activity. These events often result in non-conventional DNA termini, which must be processed before repair of the lesion can be completed. Interestingly, hereditary defects in DNA end processing often result in neuropathological disorders. Polynucleotide kinase phosphatase (PNKP), one of the DNA end processing factors, employs DNA 3'-phosphatase and DNA 5'-kinase activities to form ligatable DNA ends, and is recruited to DNA breaks via protein-protein interactions mediated by an amino-terminal fork-head associated (FHA) domain. Mutations in PNKP are associated with both *microcephaly with early onset seizures* (MCSZ) and *ataxia with oculomotor apraxia 4* (AOA4). However, how mutations in the same gene can result in two different diseases is unknown. Here, to address this question, we have begun to examine the importance of the different protein domains/activities in PNKP in human cells for DNA strand break repair, and to measure these activities in fibroblasts from patients harbouring PNKP mutations. Our current data addressing this question will be described.

Session V / 13

Single-molecule based super-resolution imaging

Sebastian van de Linde[1]

[1] *Department of Physics, University of Strathclyde, Glasgow*

Sebastian van de Linde did his PhD at the Faculty of Physics, Bielefeld University in Germany. He was working on the Photoswitching of Organic Dyes and Single-Molecule Based Super-Resolution Imaging under the supervision of Prof. Sauer. From 2011 to 2016 he was an Associate Researcher in the department of Biotechnology and Biophysics at the university of Würzburg. He did a first stay abroad in 2013 at the University of Cambridge in the Group of Dr. Kaminski and a second one in 2014 in Sydney in the Group of Prof. Kaminski. Since 2016 Sebastian van de Linde is a Lecturer and Chancellor's Fellow at the University of Strathclyde, Glasgow, Scotland.

Career advice:

- identify what you like, where your passion lies
- define a goal, focus on and work towards it
- stay curious and explore

Abstract:

Fluorescence microscopy is the method of choice to study biological samples in a comparatively non-invasive way. The field has received a powerful boost with the development of super-resolution imaging methods, which overcome the limitations imposed by optical diffraction.
A very strong class of these novel techniques can be merged under the generic term single-molecule localization microscopy (SMLM), which relies on the detection of single-molecules, their precise localization and the reconstruction of an artificial super-resolution image. It can improve on the ~200 nm resolution limit by a factor of ten and more, and thus has opened the door for the study of finer cellular ultrastructure.
While in the early days the focus was on methodological advancement, such as characterization of fluorophores and engineering of multicolour and 3D imaging capabilities, in recent years SMLM is increasingly applied in biology and medicine. Besides its high spatial resolution SMLM also provides access to quantitative information and thus enables the study of structure-function relationships.
I will provide a concise overview of the development and underlying principles of SMLM with an emphasis on dSTORM, describe novel technical developments and conclude with applications in the field of neurobiology.

Session V / 24

Career Panel

Session VI / 18

Emergent properties of model membraneless organelles

Tim Nott[1]

[1] *Department of Biochemistry, University of Oxford, Oxford*

Timothy Nott did his PhD on molecular structure at the National Institute for Medical Research in London under the supervision of Dr. Smerdon. He graduated in 2009 and moved to Toronto to study the principles of how cells are internally compartmentalised in the group of Professor Pawson. He started as Postdoctoral Research Associate in 2014 (Professor Baldwin) at the university of Oxford

before becoming a Sir Henry Dale fellow in 2016 in the department of biochemistry (University of Oxford). Timothy Nott is interested in compartmentalisation via Liquid-liquid phase separation in cells.

Career advice

• Find yourself a mentor. If you get lost in a research project or are conflicted about a career decision, a mentor who can give you the long view will be invaluable.
• Be proactive. Talk to scientists outside your immediate lab, institute, or field of expertise.
• Keep your eyes open and be prepared to act quickly. You never know where a good career/project/collaboration opportunity will come from or what form it will take.

Abstract

Condensation of cellular material into phase-separated liquid-like droplets has emerged as a fundamental new organising principle in cell biology. The dynamic and membraneless compartments formed in this way are predominantly associated with processing nucleic acids and are indispensable for cellular function. Surprisingly, we know little about the solvent environment inside these and other cellular bodies, yet it is likely to have a significant influence on the biochemical reactions that take place within them.

One important class of enzymes that are biochemically active inside membraneless organelles are DNA and RNA helicases, which remodel the structures of nucleic acids. In addition to ATP-dependent catalytic domains, several helicases possess intrinsically disordered regions that readily undergo liquid-liquid phase separation in cells and in vitro. We have recently found that model membraneless organelles reconstituted from only the disordered tails of the DEADbox helicase Ddx4 display emergent biochemical properties. Among these are the ability to selectively absorb RNAs based on their structure, and the destabilisation of nucleic acid duplexes. We hypothesise that in the context of a membraneless organelle, these properties could complement the catalytic activity of the helicase domain.

Here we show that the emergent biochemical properties of membraneless organelles formed from only the disordered tails of DEADbox RNA helicases can be tuned by their amino acid sequence, and subtle changes to their surrounding environment. These results suggest novel ways in which cells could modulate the intrinsic properties of membraneless organelle interiors to achieve specific biochemical outcomes.

Session VI / 8

Buffering protein noise by liquid-liquid phase separation

Adam Klosin[1] ; Florian Oltsch[2] ; Christoph Zechner[2] ; Anthony A. Hyman[1]

[1] *MPI-CBG*

[2] *MPI-CBG, CSBD*

The processes that contribute to protein expression are subject to stochastic fluctuations and are affected by the environment in which they operate. As a result, concentration of a given protein can vary greatly between organisms, cells, as well as in time. Since many biological processes demand a tight control over protein concentration, cells have evolved various mechanisms to control the degree of concentration variability often referred to as noise. The best studied mechanisms for buffering protein expression levels rely on feedback through transcriptional regulation. Such regulation systems are slow and can reduce the expression noise only to a certain level. Here, we explore the potential for a phase separated organelle to buffer the noise in protein concentration at the post-translational level. Based on a simple thermodynamic model, we predict that liquid droplets function as dynamic reservoirs which can buffer variations in a highly effective and near-optimal manner. Using an engineered fluorescent protein that forms liquid droplets in the nucleus of Hela cells we show that phase separation attenuates variations in protein concentrations by up to a 100-fold. We propose that phase separation could be a common strategy for achieving stable protein concentrations in cells.

Session VI / **6**

How the human neocortex folds - a novel role of the extracellular matrix

Katherine Long[1]

[1] *MPI-CBG*

Neocortical expansion is thought to underlie the cognitive traits that are unique to humans. This evolutionary expansion is accompanied by cortical folding, which starts to form from around gestational weeks (GW) 20. However, what causes it remains largely unknown. Extracellular matrix (ECM) has been previously implicated in neocortical expansion and here we investigate the potential role of ECM in the formation of neocortical folds. We focus on three specific ECM components localized in the human fetal cortical plate: hyaluronan and proteoglycan link protein 1 (HAPLN1), lumican and collagen I (collectively, HLC). Addition of HLC to cultures of human fetal neocortex (11-22 GW) caused local changes in tissue stiffness, induced cortical plate folding, increased hyaluronic acid (HA) in the cortical plate and required the HA-receptor CD168 and its downstream ERK signaling. Importantly, loss of HA reduced HLC-induced and 22 GW physiological nascent folds and this process was altered in samples with neurodevelopmental disorders, indicating it may be a useful system to study such disorders.

Session VII / **20**

Complex Spatial Networks and Programmed Shape Selection: Topology and Geometry in Biology

Carl Modes[1]

[1] *MPI-CBG, CSBD*

Carl Modes did a PhD in Physics and Astronomy at the University Pennsylvania, Philadelphia. In 2008 he started as a Postdoctoral Research Associate in the Theory of Condensed Matter Group at the University of Cambridge. In 2011 he moved back to the United States as a Postdoctoral Associate. He was working at the Center for Studies in Physics and Biology (The Rockfeller University) until 2017. Since 2017 Carl Modes is a group leader at MPI-CBG.

Career advice:

• Be aware of the Impostor Syndrome: Fight it, struggle with it, but don't hesitate to talk about it with your peers; its an incredibly common issue among scientists.
• Be brave: No job is too good to apply to if you believe you could fit there
• Cast as wide a net as possible: Remember that the whole job hunt is a numbers game. But if you can't imagine being happy at a place, for whatever reason, then don't bother with them.
• Think critically about the advice you receive: Survivorship bias is very real and even people that mean well can fall prey to it.

Abstract:

Nature finds the means to leverage complex geometric and topologic effects in many ways that are we only now beginning to understand. For example, in the case of topology, natural transport webs are frequently dominated by dense sets of nested cycles; the architecture of these networks – the topology and edge weights – determines how efficiently the networks perform their function. We present a new characterization of these physical networks that rests on an abstraction of a physical tiling in the case of a two dimensional network to an effective tiling of an abstract surface in space that the network may be thought to sit in. This new algorithmic approach can be used for automated phenotypic characterization of any weighted network whose structure is dominated by cycles, such as, for example, mammalian vasculature in the organs, the root networks of clonal colonies like quaking aspen, and the force networks in jammed granular matter. On the geometric side of the ledger, it has recently been more and more appreciated that developing biological systems employ

complicated 2D stress fields during early onset of morphogenesis from flat or quasi-flat epithelial sheets to a rich zoo of fully three dimensional objects. We discuss a speculative approach based on methods from the physics of exotic shape-shifting materials to reduce the complexity of the interacting "parts" of the stress distribution to model these developmental morphomechanics in a parameter space of drastically reduced dimensionality.

Session VII / 5

Dilute molecular crowders enhance activity of ligase ribozyme

Mrityunjoy Kar[1] ; Juan Manuel Iglesias Artola[1] ; Oliver Beutel[1] ; Alf Honigmann[1] ; Moritz Kreysing[1]

[1] *MPI-CBG*

The RNA world hypothesis remains a hallmark in *origin of life* research despite very poor robustness and low reactivity of most model replicators studied so far.[1] A frequently used trick to enhance ribozyme activity is the use of high concentration molecular crowders (M to mM) to increase RNA concentrations by excluded volume effects.[2] Here we show, that excluded volume effect is not strictly required to enhance ribozyme activity using R3C ligase as a model ribozyme and polyethylene glycol (PEG) as a model crowding agent. As observed in other systems before, we found that also for the R3C system reactivity is increased in presence of crowder. However, our data shows higher affinity (lower Km) at lower concentrations of crowder (1% wt/v). This suggests that excluded volume might not be the only effect. If so, enhanced activity should also be seen at even lower concentrations of crowder. Indeed, we found in our experiments a remarkable enhancement of R3C ligase activity at concentrations down to 50ppm (wt/v). With this, we suggest a beneficial role of polymeric crowders (impurities) during the origin of life.

Closing Session / 25

Postdoc Association Meeting